THESIS
FOR THE AWARD OF DEGREE OF DOCTOR OF MEDICINE SESSION 2022-2025

Drug Utilization Pattern of Antidepressant Drugs among patients with Depressive Illness attending Psychiatry OPD in a Tertiary Care Teaching Hospital

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ACKNOWLEDGEMENT

With profound gratitude, I thank the Almighty God for His endless blessings, guidance, and strength, without which this journey would not have been possible.

I am profoundly grateful to my guide, **Dr. Shaktibala Dutta**, Professor of Pharmacology, for her invaluable mentorship, patience, and unwavering support. Her insightful guidance has played a pivotal role in shaping this research. My sincere thanks also go to my co-guides, **Dr. Rajni K Rai** and **Dr. Brijesh Saran**, for their expertise, motivation, and continuous encouragement. I am equally thankful to **Dr. Saborni Dey**, Head of Department, for fostering a positive academic environment and always pushing me to excel.

A special thanks to my dear friends, as well as my seniors, juniors, and batchmates, for their constant motivation and who have made this journey memorable. I also acknowledge the supporting staff for their invaluable assistance.

Beyond academics, I am forever indebted to my family. My father, **Shri Ashok Kumar**, whose silent strength and encouragement have always been my backbone. My brother, Ajay, for being my pillar of support, my source of motivation, and my biggest cheerleader. My little angel, Nyra, whose love and laughter bring meaning to every struggle. And my husband, **Dr. Ameet Mohan Rathod**, for his unwavering support and belief in me.

This work is lovingly dedicated to my dearest mother, **Smt. Saroj Devi**, whose unwavering love, sacrifices, and belief in me have been my greatest source of strength.

Lastly, I would like to acknowledge the participants of this study for their time and cooperation without which this research would not have been possible

This thesis is a reflection of the love, support, and guidance I have received, and I remain deeply grateful to each and every one of you.

Dr. Navreet

ABBREVIATION

S. No.	Abbreviation	Full Form
1.	ADHD	Attention Deficit Hyperactivity Disorder
2.	ADR	Adverse Drug Reaction
3.	AIIMS	All India Institute of Medical Science
4.	APA	American Psychiatric Association
5.	ASD	Autism Spectrum Disorder
6.	BPRS	Brief Psychiatric Rating Scale
7.	BZD	benzodiazepine
8.	CBT	Cognitive behavioural therapy
9.	CDSCO	Central Drugs Standard Control Organizations
10.	COVID	Corona Virus Disease

11.	DALYs	Disability adjusted life years
12.	DDD	Define Daily Dose
13.	DPCQ	Doctor-Patient Communication Questionnaire
14.	DRPs	Drug Related Problems
15.	DSM	Diagnostic and Statistical Manual of Mental Disorder
16.	DUR	Drug utilization research
17.	ECT	Electro convulsive therapy
18.	EML	Essential Medicine List
19.	EPS	Extra Pyramidal Symptoms
20.	FDC	Fixed Drug Combination
21.	FGA	First-Generation Antipsychotics
22.	GAD	Generalized anxiety disorder
23.	HAM-D	Hamilton Depression Rating scale
24.	ICD	International Classification of Diseases
25.	IEC	Institutional Ethics Committee
26.	INURD	International Network for Rational Use of Drug
27.	IPD	In Patient Department

28.	IPS	Indian Psychiatric Society
29.	ISMI	Internalized stigma of Mental Illness
30.	MAOI	Monoamine oxidase inhibitors
31.	MARS	Medication Adherence Report Scale
32.	MDD	Major depressive disorders
33.	MPR	Medication-Possession-Ratio
34.	NCR	National Capital Region
35.	NICE	National Institute of Health and Care Excellence

36.	NLEM	National List of Essential Medicine
37.	NMC	National Medical Commission
38.	OCD	Obsessive compulsive disorder
39.	OPD	Out Patient Department
40.	PDD	Persistent depressive disorder
41.	PDD	Prescribe Daily Dose
42.	pDDI	Potential Drug-Drug Interaction
43.	PTSD	Post traumatic stress disorder
44.	PWMD	Person with Multiple Diorders
45.	QOL	Quality of Life
46.	SGA	Second-Generation Antipsychotics
47.	SNRI	Serotonin norepinephrine reuptake inhibitor
48.	SPSS	Statistical Package for the Social Sciences
49.	SSRI	Selective serotonin reuptake inhibitor
50.	TCA	Tricyclic antidepressant
51.	USA	United States of America
52.	WHO	World health organisation
53.	YMRS	Young Mania Rating Scale

CONTENTS

SERIAL NO.	INDEX	PAGE NO.
1.	INTRODUCTION	1-6
2.	AIM AND OBJECTIVES	7
3.	REVIEW OF LITERATURE	8-27
4.	MATERIAL AND METHODS	28-32

5.	RESULTS	33-46
6.	DISCUSSIONS	47-52
7.	SUMMARY & CONCLUSIONS	53-54
8.	REFERENCES	55-61
9.	ANNEXURES 1- PLAGIARISM CERTIFICATE 2- ETHICAL CLEARANCE 3- CONSENT FORM- ENGLISH 4- CONSENT FORM- HINDI 5- DATA SHEET	62-66

LIST OF TABLES

Table No.	Details	Page No.
1.	Sociodemographic characteristics of the participant attended psychiatry department	34
2	Clinical characteristics of the patients attended psychiatry department	35
3	Antidepressant drug usage pattern of the patients attended psychiatry department	36
4	Gender wise distribution of HAM-D & MADR Score of severity of depression in patients attended psychiatry department	36
5	Adverse effects produced by Antidepressant drug used in the patients attended psychiatry department	37
6.a	Association of severity of depression score with gender ANOVA	42

6.b	Association of severity of depression score with gender ANOVA (Bonferroni Post-hoc-Tests RM Factor	42
7	Association of severity of depression score with gender using t - test	45
8	Analysis of Antidepressant prescriptions based on WHO core drug use indicators	46

LIST OF FIGURES

Figure No.	Details	Page No.
1.	Percentage of antidepressant drugs used in the study	39
2	Depicting adverse effects by particular medication	40
3	Depicting adverse effects by particular medication	41
4	Depicting HAM-D and MADR score at admission & follow-up of 6 weeks of antidepressant treatment	42
5	Decreasing pattern of HAM-D and MADR score at follow-up of 6 weeks of antidepressant treatment in male & female patients	43
6	Decreasing pattern of HAM-D score at follow-up of 6 weeks of antidepressant treatment by particular antidepressant medications	44
7	Decreasing pattern of MADR score at follow-up of 6 weeks of antidepressant treatment by particular antidepressant medications	45

8	Pattern of severity of depression score in different income group	46
9	Distribution of cost (INR) in prescription following NLEM (2022) for antidepressant medications	49
10	Distribution of Route of drug administration in prescription following NLEM	50

INTRODUCTION

INTRODUCTION

Drug Utilisation Research

Drug utilisation research (DUR) is defined by the World Health Organisation (WHO) as a study that focusses on the marketing strategy, distribution, prescription, and usage pattern of pharmaceuticals within a health care system of a specific epidemiology. The study also places a particular emphasis on the social, medical, and economic repercussions that result from the practice. Within the context of this kind of research, it is necessary to collect quantitative data concerning the extent, variability, and costs associated with medication therapy. In terms of its nature, it can be either qualitative or quantitative [(1)]. When it comes to clinical practice, DUR study is extremely important because it provides a comprehensive picture of how various medications are used and assists in identifying areas that need to be improved. A determination is made regarding the justifiability of prescriptions [(2)]. A World Health Organisation report states that nearly half of all medications are either prescribed or administered in an incorrect manner. The utilisation of such an unnecessary drug may lead to therapeutic outcomes that are not satisfactory. It is of the utmost importance to investigate these prescription patterns in order to strengthen and improve appropriately prescribed practices. [(3)]. There are a number of factors that have contributed to the rise in interest in DURs [(4)], including the growing awareness of the virtually explosive growth in the marketing of new pharmaceuticals, the vast differences in prescription and consumption habits, and the mounting worry over the cost of medications.

Background of the study

Mental and behavioural disorders constitute almost twelve percent of all diseases worldwide. This area encompasses a diverse range of ailments, including affective disorders, schizophrenia, depressive disorders, and obsessive-compulsive disorders (OCD) [(5)]. Psychiatric disorders account for four of the most prevalent health issues leading to disability-adjusted life years (DALYs). The health care systems of most impoverished countries are incapable of delivering even basic mental health care. Mental illness is significantly correlated with the usage of health services and pharmaceuticals, resulting in substantial costs that predominantly constitute a financial burden on the patient. This is particularly applicable in poorer nations. The WHO2001 (WHO 2001a) recommends promoting the accessibility of a select few critical psychiatric medications.

This recommendation is among several proposed to enhance the care provided to individuals with multiple conditions. Their relevance in public health institutions, the pursuit of data on efficacy and safety, and the comparative costeffectiveness of outcomes are all variables considered during the selection process [6]. Essential psychotropic medications are recognised for their capacity to address the population's paramount mental health care needs. Utilising all drugs deemed "effective" for the treatment of mental diseases is not invariably "essential" [7].

Pharmacotherapy for psychiatric disorders is often linked to adverse drug reactions (ADRs). The risk of ADRs in a patient may be heightened when many drugs, referred to as polypharmacy, are necessary for symptom management. Most psychiatric disorders lack a permanent cure and necessitate lifelong care. Research indicates that adverse event reporting in published trials lacks reliability. Consequently, psychiatrists must comprehend the notion of identifying and reporting probable adverse medication responses.

The WHO defines "medication non-adherence" as a situation where an individual's medication-taking behaviour does not align with the prescriptions provided by healthcare providers. Patients with serious psychiatric disorders are more prone to poor reasoning and diminished insight due to the nature of their illness and the therapy they are undergoing. The outcome is that individuals are less inclined to comply with the drug regimen given by their physician [8]. A patient's condition may worsen, treatment may become less successful, or the patient may exhibit diminished responsiveness to subsequent interventions if they fail to comply with prescribed psychiatric medication regimens. Non-adherence to treatment can lead to several adverse outcomes, including an elevated risk of suicide, a greater prevalence of co-morbid medical conditions, increased rates of re-hospitalization, diminished quality of life or psychosocial outcomes, symptom recurrence, and inefficient use of healthcare resources.[9] To develop effective interventions and attain treatment objectives for patients and healthcare providers, it is crucial to investigate the prevalence of psychotropic drug usage among individuals with severe mental illnesses, alongside safety concerns, nonadherence, and related factors. This study seeks to monitor, assess, and, if warranted, propose modifications to prescribing procedures to enhance the rationality and affordability of healthcare. The utilisation pattern of mental medications will be monitored during this study. Consequently, it is imperative to perform regular evaluations of drug usage habits to

ensure that treatment remains both safe and effective. The data originates from public hospitals and reflects the distinct prescribing procedures characteristic of these institutions. Significant disparities exist between research practices and real-world applications, whereas the prescribing of drugs for psychotic disorders is perpetually developing. [10]

The Hamilton Depression Rating Scale (HAM-D), especially the 17-item variant, is a commonly utilised instrument in therapeutic trials for MDD. It assesses both somatic and psychological symptoms, although there are certain psychometric and content validity concerns. The HAM-D17 exhibits strong reliability, convergent and discriminant validity, and sensitivity to change; however, its multidimensional structure may influence its responsiveness. Response and remission are commonly evaluated using this scale, with remission characterised as < 7 or occasionally ≤ 2. The Montgomery–Åsberg Depression Rating Scale (MADRS) is an essential instrument for assessing the efficacy of antidepressants, concentrating on psychological symptoms. It demonstrates robust internal consistency, convergent validity, discriminative ability, and sensitivity to change, with remission thresholds ranging from ≤ 4 to ≤ 10 points.[11]

The pharmaceutical treatment of depression includes several classes of antidepressants: MAOIs, SNRIs, TCAs, SSRIs, and atypical antidepressants. The widespread prescription of sertraline, duloxetine, mirtazapine, and escitalopram underscores their predominance, accounting for 96.36% of antidepressant utilisation. Effective care of depression requires a personalised strategy, taking into account symptomatology, medical history, and concurrent psychiatric disorders. This frequently results in antidepressant polypharmacy, wherein prescription combinations are customised to meet the individual requirements of patients[12]. Moreover, primary care screenings act as a conduit for the prescription of antidepressants, particularly for elderly patients who may undergo prolonged antidepressant treatment. The primary intervention for depression, as per guidelines of the NICE- National Institute for Health and Care Excellence, in 2009, emphasises evidence-based psychological therapies, notably cognitive-behavioral therapy (CBT). Based on empirical evidence, cognitivebehavioral therapy seeks to alter detrimental thought processes and behaviours linked to depression. Its efficacy has been extensively documented in numerous research, demonstrating the potential to reduce symptoms and improve general well-being[13, 14]. Antidepressants are advised when early psychological therapy are inadequate or in instances of severe depressed symptoms. For

individuals aged 18 and older, these can provide substantial symptom alleviation and enhanced quality of life. Decisions about the initiation of antidepressants should entail collaboration among the patient, family or carer, while considering the potential advantages, hazards, and alternatives. In children and adolescents, antidepressants serve as a second-line treatment for moderate to severe depression, although initial administration for severe instances necessitates evaluation by a child and adolescent psychiatrist. The application within this group presents safety issues, possible adverse consequences, and the requirement for diligent oversight[15].

The duration of recommended antidepressant medication is contingent upon patient history and the risk of relapse. It is recommended to administer maintenance treatment for a minimum of two years following the remission of symptoms in cases of recurrent depression. Nonetheless, data suggests prolonged usage of antidepressants beyond this period, prompting enquiries regarding their appropriateness. The increased frequency of antidepressant prescriptions in the UK has elicited examination over their safe and beneficial use. Complexities arise from diversity in individual responses, patient experiences, and issues such as long-term usage and withdrawal management, with termination potentially resulting in withdrawal symptoms[16]. In the last ten years, there has been a significant rise in economic assessments aimed at preventing mental diseases and improving mental health. Although numerous initiatives in this domain demonstrate favourable cost-effectiveness, the variability in evaluation quality and methodologies limits generalisable conclusions. Nonetheless, the promising trend of favourable value for money, especially among children, adolescents, and adults, underscores promise. However, additional study is required to evaluate costeffectiveness in low to middleincome contexts. Their research also examines the mental health aspect of the WHO's CHOICE project, intending to furnish costeffectiveness evidence for interventions addressing significant factors to disease burden. Current modelling encompasses therapies for schizophrenia, bipolar disorder, depression, and panic disorder. Costeffective treatments arise for prevalent mental diseases, although community-based interventions for severe cases satisfy costeffectiveness standards. These findings provide critical insights for policymakers, facilitating informed investment decisions in psychiatric care and addressing obstacles to successful burden management[17]. Due to the unique healthcare environment and resource distribution in India, it is essential to undertake drug utilisation studies in tertiary healthcare facilities.

These investigations offer insights on trends of antidepressant usage, dose, treatment duration, and related expenses. By thoroughly evaluating these elements, the studies enhance informed clinical judgements and pharmacoeconomic assessments. Furthermore, they recognise treatment adherence deficiencies and direct treatments for optimal patient outcomes, thereby improving both evidence-based psychological therapy and antidepressant strategies. Recognising the necessity for such studies within India's tertiary healthcare framework might develop pharmacoeconomic understanding, influence healthcare policies, and ultimately improve patient care.

Significance of the Study

For the purpose of improving clinical practices in psychiatry at a teaching hospital like Santosh Medical College and Hospital, this study has provided valuable data that can be used for the purpose of service planning. Among patients who were receiving treatment at mental health facilities in the National Capital Region of Delhi, the study documented the extent of comorbidities that are associated with mental disorders, the safety of medications that were prescribed, and the degree and degree of adherence to treatment from those patients. Therefore, the findings of this study have successfully addressed a number of knowledge gaps. The results that were obtained will be utilised by subsequent researchers in order to validate their own discoveries with regard to the results that will be obtained in the future. The findings and interpretations of this study can be put to use in the context of healthcare settings for the purpose of managing the clinical outcomes of patients. It is possible that improving treatment outcomes will result in a reduction in the overall burden that is associated with mental healthcare. As a consequence of this, the burden of physical and emotional stress that is imposed on patients, their families, carers, and other individuals who are involved will be reduced.

This will be a positive development.

DUR of the tertiary institute conducted this study with the intention of serving as a review of a variety of various health programs. Therefore, it laid the foundations for stakeholders of mental health care in institutions that primarily provide psychiatric care and are located in the National Capital Region (NCR) to analyse specific outcomes of their efforts, particularly in relation to treatment compliance. This was accomplished by establishing the foundation. The establishment of a framework for the evaluation of certain outcomes was the means by which this objective was accomplished. After the

task at hand has been completed, it is of the utmost importance to put the appropriate strategies into action in order to reach supremacy and rationality in prescriptions. It is strongly suggested that these strategies be implemented in order to maintain excellent practices on a consistent basis and to address areas that have room for development. Our DUR study will contribute to the development of policies, programs, strategies, and projects that are related to evidence-based medicine. The overarching objective of these endeavours is to improve the overall satisfaction of patients as well as their quality of life.

The implementation of efficient policies has the potential to facilitate the incorporation of patient-centered approaches in mental healthcare, thereby recognising the patient as an essential element in the process. When it comes to determining the most effective course of action, stakeholders are confronted with uncertainty and a lack of guidance on how to proceed because there is no policy that has been prepared based on evidencebased practices.

All of the other parties involved in mental healthcare would benefit from the findings of our study, which would be beneficial in supporting patients for their treatment and their families for compliance when it comes to mental healthcare.

These recommendations, if put into action, will be of great assistance in advancing the well-being of patients as well as the families of those patients. This study has the potential to lay the groundwork for future clinical interventions that will be carried out by psychiatric specialists in collaboration with individuals who are committed to addressing the challenges that individuals who suffer from mental disorders face and the well-being of those individuals. In light of this, DUR studies concerning the utilisation of antidepressants drugs are an urgent necessity in the tertiary care centre. Understanding drug utilization patterns in mental health is crucial for promoting rational medication use, enhancing effectiveness, and minimizing adverse reactions and unnecessary expenses.

AIM & OBJECTIVES

Chapter 2

AIM & OBJECTIVES

Aim

To analyse the Prescription patterns of Antidepressant medications among individuals diagnosed with Depressive Disorder who are visiting the Psychiatry OPD at a Tertiary care Teaching Hospital

Objectives

- To evaluate the pattern of medication, use by using WHO-CORE indicators

- To observe the clinical outcome based on clinician-rated
  a. HAM-D: Hamilton Depression Rating Scale &
  b. MADRS: Montgomery and Asberg Depression Rating Scale

- To observe their safety profile of these drugs by assessing Adverse Drug Reactions

- To evaluate the cost-effectiveness by direct cost evaluation of these drugs

REVIEW OF LITERATURE

Chapter 3

REVIEW OF LITERATURE

According to the Global Burden of Disease Study from the WHO, psychiatric disorders are considered to be the among the most burdensome diseases in the world. Among psychiatric illness, depressive disorder including anxiety disorders are the most prevalent mental health problem, lead to impact more than 15% of individual at certain phase during their entire lives. Depressive disorder especially (MDD) has been reported as the 3rd cause of the burden of disease worldwide in 2008 by a report of WHO, which has been assumed that this disease will rank first by 2030 and drive-up health service utilization & their associated costs. Depression encompasses a spectrum of emotional and cognitive disturbances, including feelings of melancholy, loneliness, misery, and diminished self-esteem. The profound impact of depression is evident in its prevalence and its association with severe consequences, such as suicide attempts, affecting 10–15% of individuals with severe depression[(18)].

Depressive disorder marked by various distressing symptoms, it has become a major public health issue worldwide. Here in this chapter, we seeks to explore the various dimensions of depression, its prevalence rate, treatment modalities covered, and the pharmacodynamic of antidepressant drugs in addressing this debilitating condition. Furthermore, it highlights the important necessity of conducting medication usage studies at tertiary healthcare facilities among the Indian population especially in NCR. These studies are primarily intended to improve pharmacoeconomic insights and clinical decision-making to manage depressive illness. A variety of mental and emotional problems, such as melancholy, feelings of loneliness, hopelessness, and a diminished sense of self-worth, are included in the category of depressive disorders. Sometime adjustment problem also presented in the outpatient department as depressive sign. The other clinical manifestations of depression include prolonged episodes of melancholy, which are always accompanied by feelings of mistrust, anxiety episode, impaired-concentration, diminished attention span, cognitive lethargy, sleep disturbances, significant weight changes, altered eating behaviours, psychomotor agitation or retardation, persistent feelings of guilt or worthlessness.

There are a marked reduction in energy or libido, also seen that all of which continue for a minimum of at least two weeks[18].

Prevalence rate of the disease

The prevalence of mental illness increases steadily in all geographical areas, along with neuropsychiatric disorders, which accounts for around 14% of global pollution. Over the next few decades, depression is expected to be the main causes of disability and the main causes of disability in developed countries, including the United States. In New Zealand, the incidence of depression increased by 35% over five years. Depression is observed in young people, with a prevalence of 0.4% to 2.5% in elementary school students and 0.4% to 8.3% in young people. The life prevalence rate of major depression in South Africaregion is estimated to be nearly 9.7%, which corresponds to a global trend[19,53].

Factors associated with depressive disorder

Stress is often associated with the development of depression. People's sensitivity differs significantly compared to mental illnesses, including depression. Diatom stress models explain this diversity by examining factors such as vulnerability (polarization) and trigger stressors (stress). This model shows that while an increase in diatoms correlates with a reduced level of stress required to trigger depressive episodes, the occurrence of such episodes increases the expression of potential future episodes. Psychological, behavioral related, and biological factors contribute to the mechanisms in which early life experiences develop the likelihood of depression by transforming these traumatic experiences into permanent weaknesses. The method of information processing is influenced by childhood events. For example, ubiquitous negative thoughts observed in people with depression often reflect harmful cognitive frameworks developed through adverse childhood experiences, such as criticism, depression parents, and rejection. People who encounter important unwanted life events like mourning are at a higher risk of starting a depression episode. This risk can be attributed to convene with small events such as poverty, family inconsistency, unemployment, chronic illness, or unintended pregnancy. Another factor reflected and inherited in early life experiences are personality traits that contribute to the development of depression in relation to social and cognitive

factors. Neuropathy, a personality trait, is the most important risk- factor for depression, affecting the effects of genetics and early childhood experiences on persistent depressive symptoms. This physiological system involves the production of adrenal cortical structure hormone(ACTH) by the hypothalamic glands and secretion of CRH,(corticotropinreleasing hormone) from the paraventricular core of the hypothalamic region by the release of glucocorticoids. Adrenal cortex cortex from adrenal cortisol and adrenal abdominal cortex cortisol. Cortisol secretion has negative feedback regarding the hypothalamus and regulates HPA axis activity. A descending path from the amygdala transmits emotional impulses to the HPA axis, which leads to stimulating effects. The hippocampus controls the HPA axis through a negative feedback loop, with cortisol inhibiting the HPA axis. Lack of inhibitory regulation of the HPA axis. A long loss of sensitivity to GR can lead to a deferred effect on the HPA axis, which leads to serious consequences such as the production of neurotoxic free radicals due to over-activity of calcium-dependent enzymes, reduced production of brain-derived- neurotrophic factor BDNF, as well as glucose transport. This study showed a decrease in BDNF mirrors when long stress expositions occurred, resulting in lower BDNF in the hippocampus of people who died from suicide. Chronic exposure to thecortisol has been shown to increase the activity of MOAA, the enzyme responsible for the degradation of monoamine noradrenaline and serotonin. Neuroimaging studies continue to support this by showing increased MAO-A activity in the brains of people with depression. Their data supports the idea of serotonin reduction and Nordrenal testing in people with depression. Chronic exposure to glucocorticoids induces neurochemical and structural changes in the hippocampus that closely mimic the observations observed in patients with depression. Longer exposure to increased glucocorticoid levels can harm several brain regions, including the prefrontal cortex, in addition to hippocampal damage. Prolonged exposure to stress and increased cortisol levels were associated with anhedony experienced by people with depression. Anhedney is unable to enjoy joy and present basic signs of depression. This condition is associated with a reduced activity of the mesoperiosteal DA from the ventral compression region (VTA) to the nucleus accumbens. Like other depressive symptoms, anhedony can also correlate with reduced hippocampal activity[(20)].

Relation to Adverse effect

Important research has shown that negative childhood experiences, such as sexual, physical, verbal abuse and exposure to care, contribute significantly to the development of depression in people in later years. This theory of depression, which emphasizes the effects of stressors in early childhood, presents two hypotheses that reveal the observed variation in depression in these patients. The original concept is a different exposure hypothesis, which determines that differences in relation to psychological health outcomes arise from different types of stressors. This framework posits that women exhibit a greater prevalence of depressive symptoms compared to men, attributed to their encounters with a higher frequency and distinct nature of stress-inducing events. The differential vulnerability hypothesis posits that, given equivalent levels of

exposure, individuals exhibit varying degrees of impact from that exposure in relation to depression. This variation is primarily attributable to individual factors that either heighten or mitigate vulnerability.

This indicates that women may have higher levels of depression than men, as women tend to have a greater impact on women and tend to serve as a stronger stressor for the women.

The total impact of physical-assault & abuse experienced during child-hood on adult well-being is extensively documented. Research indicates that such forms of maltreatment correlate with heightened risks of anxiety, substance abuse, depression, and mental illness, as well as an increased likelihood of being convicted of violent offences. Regarding care, there is a lack of understanding in relation to the correlation between depression and the lack of a stable parental frame.

Theories propose that comprehending the impact of foster care on an individual's life hinges on various factors, including neglect, parental substance-abuse, unstable living arrangements, & frequent transitions between carers. These elements collectively heighten the probability of adverse outcomes in adulthood, such as depression. This particular finding has been further confirmed by additional studies that point to more than 60% of the transition from 18-year old nursing to adulthood encounter at least one traumatic event, and that sexual abuse is the most common. The emergence of these traumatic events improves patient susceptibility to depression[21].

Theories of depression

The monoamine neurotransmitters NA, 5HT, and DA play a critical role in promoting transmission within neural pathways that come to the brainstem. In addition to descending projections into the autonomic nervous system, these neurotransmitters have numerous ascending projections on both the limbic system and the cortex. Various aspects of behavioral functions, including mood and fear, and pathways that exercise important control over these phenomena. Early theories suggest that monoamine deficiency plays an important role in the physiological basis of depression. This is primarily recognized as a substance that promotes the release of monoamines, such as amphetamines, to assume antidepressant effects, whereas those that interfere with

monoamine release, such as reserpine, tend to induce depressive symptoms in patients following administration. Postmortem evidence from neuroendocrine and neuropathy

studies shows that depression correlates with dysfunction in postsynaptic monoamine receptor activity. Certain antidepressants directly affect these receptors. Rich clinical and preclinical testing suggests that changes in serotonergic function may correlate with severe depressive disorders. Participation of noradrenagen and dopaminergic neurotransmission was found.

During the years of the underlying factors of major depression, it is generally recognized that dysfunction and reduced activity within the monoaminergic system is considered a major combination of contamination of symptoms associated with depression. This premise was primarily based on the observation that antidepressants improve activity and, consequently, the function of monoaminergic systems, particularly serotonin and noradrenaline. A notable feature of this elevated monoaminergic system is that their cell bodies are located in the brain stem. Its activity is thus carefully determined by the PFC, a cortical region where metabolic irregularities are observed in people suffering from depression. As a result, the locus brain, raphe nucleus, and ventral cortical regions for noradrenergic, serotonergic, and dopaminergic cell bodies are home neurons. These regions correspond to the dorsal and ventral shingles regions of the primate and human brain[21]. Electro-physiological studies of the patients have shown that the function of monoaminergic neurons is meticulously determined by these downward afferents, either directly (e.g., monosynaptics) or indirect (local intern) paths. As a result, changes in metabolism within the anterior subzonal zonal zonal zonal zonal may affect functional interactions between marginal and cortical regions, which have been proven to contribute to the use of depressive disorders. Abdominal metabolic changes often result in metabolic changes in the ventral region that can contribute to depressive symptoms, fear, effects, effects, knowledge, sexual drive, and sleep, taking into account the role of monoamines. Administration of antidepressants revives monoamine activity within the cortical and marginal regions, thus improving the relationships of depression and its impact on physiological approaches. The efficacy of antidepressants in 5HT neurons is significant. This is because the site of action in the paper frequently overlaps with that of noradrenage neurons. Serotonin release and serotonergic activity in the foreskin are meticulously regulated processes determined by various presynaptic and postsynaptic mechanisms developed during human development to maintain consistent and regular activity of serotonin neurons[28]. This indicates that antidepressants who want to improve serotonin

release disrupt homeostasis in the serotonia system, thus activating autoregulatory systems and mechanisms that limiting the full efficacy of antidepressants[22]. A considerable number of studies have focused on examining how different 5HT receptors affect both the treatment and pathophysiology of primary depression. Researchers have shown great interest in this particular receptor as they are looking for innovative ways to improve antidepressant therapy by avoiding or improving adaptation mechanisms, leading to a significant increase in extracellular serotonin levels. From all serotonin receptors tested, the 5HT1A receptor has been created as the most fascinating topic of research. With this in mind, the main reason for this is clearly why numerous postmortem and genetic testing showed that people who increased the value or activity of the 5HT1A autoreceptor may be affected by mood disorders and show a reduced response to antidepressant therapy[30]. To support this finding, testing shows that patients with recovered major depression have a reduced likelihood of 5HT1A receptor binding compared to control personnel. This observation led to the hypothesis that a decrease in 5HT1A recipe density could contribute to an increased susceptibility to primary depression. After administering SSRI or SNRI, excess serotonin participates in the Somatodendritic 5-HT1A autoreceptor, leading to hyperpolarization of 5-HT neurons. As a result, this mechanism counters the input of incoming concentrations[22]. Antidepressants induce overactivation of physiological feedback mechanisms by significantly increasing the extracellular mirror of serotonin within the raphe core, the area where the brain's serotonin transport system is the highest concentration. As a result, this leads to a decrease in serotonergic activity & the release of serotonin to the foreman. Thustheir finding could result in numerous researchers looking at ways to antagonize autoreceptors, thereby increasing the effectiveness of antidepressants. Another serotoner receptor that has attracted considerable attention from researchers is the 5-HT2A receptor.

A significant amount of literature shows that different antidepressants and gastrointestinals have strong affinities for this receptor and thus highlight the potential importance in the context of depression. Numerous clinical studies have shown that atypical antipsychotics improve clinical response to SSRIs in treatment-resistant patients. Recently performed findings show that antagonism or blocking of the 5-HT3 receptor can improve the increase in extracellular serotonin induced by SSRIcitalopram.

Furthermore, studies have shown that administration of serotonin agonists in rat brain alters important markers associated with depression, leading to increased phosphorylation of CREB proteins and promoted neurogenesis in the hippocampus [22,23].

Some antipsychotic medication for management of depression

Various studies have shown how the effects of atypical antipsychotics in existing therapeutic schemes, including antidepressants, have beneficial effects. This is particularly pronounced with administration of SSRIs observed in treatment-resistant depression. Although antidepressant therapy is observed to provide early relief and reduction in depressive symptoms in number of patients, only almost 50-60% of people diagnosed with severe depression have a favorable response to such treatment[24]. Atypical antipsychotics include olanzapine, aripiprazole, ziprasidone, quetiapine, and risperidone. These active ingredients were identified as enhancers of the effectiveness of antidepressants. Atypical antipsychotics enhance the efficacy of antidepressants through their binding affinity to serotonin receptors, which surpasses that of dopamine receptors. Additionally, they interact with histamine and adrenergic receptors, with ariprazole demonstrating a notable propensity for activity at 5-HT1A receptors[24]. **Perspectives on the societal understanding of depression**

The prevailing perceptions within society concerning mental health issues have frequently captured attention. This is primarily due to its association with stigma related to the recovery process. Mental disorders, including psychosis, schizophrenia, and depression, were often associated with increased stigma within society, along with reduced expectations for recovery. A general perspective of the public, showing considerable durability, finds that treatment for depression should prioritize priorities over biological forms or pharmacological strategies. In Germany, it has been widely accepted that the attribution of depression to “brain disease” rose from 25% to 38% between 1993 and 2001. Additionally, the percentage of cases linked to “hereditary” factors saw a modest increase from 37% to 40%. Notably, the recognition of “partnership problems” and “work stress” surged significantly, with reported increases from 73% to 81% and 75% to 80%,respectively. A study conducted in Sweden showed that 69% of people who experienced depression, current lives, mainly from work and

family duties, highlighted previous life events (32%) as the main contribution to their condition. A comparable investigation conducted in Austria revealed that the belief in "inherited or genetic" factors rose from the forty-nine percent to sixty-five percent in last sixteen years (1995-2011). The study identified "day-to-day problems," "the death of a close friend or relative," and "childhood issues" as significant contributors to depression. Research indicates that individuals experiencing depression are significantly more inclined to attribute psychosocial stress as the underlying cause of their condition, in contrast to the perspectives of those who are not depressed. Furthermore, patients who have undergone treatment for depression demonstrate a heightened tendency to identify socialisation factors, such as negative childhood experiences, as contributing elements, while being less likely to consider biological factors as causative agents of their depression. Nevertheless, patients with depression tended to be due to psychosocial stressor conditions rather than the biological or the genetic effects, although not to a lesser extent than the general population as the underlying causes of depression[25]. This indicates that people with depression are increasing awareness of the importance of biological factors compared to the general population. This manual helps classify different forms of depression and promote a more accurate approach to therapeutic intervention. At least five of the nine symptoms listed below should be present at a pronounced frequency that occurs almost daily. Symptoms of these conditions include: The ubiquitous presence of melancholy or irritability experienced in a significant part of the day. 2. Significant reduction in enjoyment and involvement in various daily activities. 3. Changes in appetite. This leads to an astonishing weight change (5%)4. Either a form of sleep disorder, insomnia or hyperpathy. Psychomotor delay or upset 6. Vitality fatigue and fatigue 7. Unjust guilt or inadequate feeling 8. I'll accompany you. 9. Persistent ideation regarding selfharm or mortality[25]

Dysthymic disorder Dysthymic disorder represents a chronic form of depression characterised by enduring physical and cognitive symptoms akin to those of major depressive episodes, albeit with a lesser intensity yet prolonged duration. The DSM-V manual delineates the diagnostic criteria for dysthymic disorder in the subsequent manner:

A diagnosis is established when an individual has endured a persistently low mood for the entire day, occurring on a nearly daily basis, and lasting for a minimum duration of 2

full years. These factors encompasses the manifestation of two or more of the following mentioned symptoms, which have resulted in considerable disruption to social or occupational functioning:

- Alteration in appetite.
- Disrupted sleep patterns manifest as either insomnia or hypersomnia.
- Reduced vitality or exhaustion. Diminished self-worth.
- Challenges in maintaining focus or encountering obstacles in the decisionmaking process.
- Experiences of despair[25].

Mood Disorder Induced by Substance Use

A substance-induced mood disorder is characterised by a persistent and significant alteration in mood resulting from the direct-physiological impact of exposure to a substance. So this particular category of mood disorders is often observed in people dealing with rehabilitation or treatment for substance abuse. Mood disorders include depression mood states, mania episodes, or a combination of both. This disease only manifests during substance withdrawal or addiction, indicating an abbreviated trajectory compared to other depressive disorders[26].

Adjustment Disorders with Depressive Moods

Depressive symptoms that result from this special disorder are caused by intensive emotional place or psychological stress. Stress factors that make it a recurring or unique event can occur in the form of family inconsistencies, marriage resolution, professional retreat, or loss of a loved one. Acute adjustment disorders can remain for several months, but chronic adjustment disorders can clearly be maintained after filling in the initial stressor. However, symptoms of this disease are not relatively severe than symptoms associated with severe depressive disorders, and have similarly extended periods of time that are characteristic of sympathetic disorder disorder. This form of depression occurs as a result of underlying diseases such as Parkinsonion disease and hypothyroidism.

Major symptoms of this special form of depression include:

Delayed development of depressive symptoms

- Recognition of existing medical diseases.

- Unconventional symptoms of specific psychiatric diagnosis - Lack of history of personal and family mental illness - Use of prohibited substances.
- Drug administration.
- Resistance to treatment or atypical response to therapeutic interventions.
- Abrupt occurrence of psychological symptoms.
- Vital sign deviation can reveal yourself as a fundamental symptom of a variety of mental disorders, includes PTSD, cases of schizophrenia disorder, and many anxiety disorders, agoraf, social disorders, & general anxiety.[27]

Treatment modalities of depressive illness

Patient treatment develops as a systematic step-by step process. The following text describes tentative patient management proposals, as clarified by the American Psychiatry Association 2010).

- Forging and support of the Treatment Alliance will participate in the patient. This takes individual factors and preferences into consideration when deciding on the appropriate treatment course.
- The fulfilment of the psychiatric assessment entails the thorough collection of the patient's history, encompassing both a general-medical-history and a psychiatric -history. This considers a mental status examinations, an exploration of the family history concerning mental disorders, and an evaluation of the individual's responses to significant life events.
- **Patient Safety Assessment** –

A careful assessment of suicide risk is conducted for each individual patient. The patient is assessed for the possibility of harming herself or others. In addition to all the underlying illnesses that can increase the tendency to deal with such thoughts, suicide thoughts, attempts and strategies are recognized. The assessment includes the patient's hydration status, selfcare practices, and nutritional intake.

- Create a treatment friendly environment. This ensures patient safety and at the same time promotes improvement without undue limitations.

- Quality of life and assessment of all dysfunction. As well as identifying existing dysfunctions in regards to patient commitments, educational activities, and patient commitments to family interactions, an assessment will be conducted.
- Become interdisciplinary collaborations with relatives from other health professions to ensure comprehensive patient care.
- Assess the patient's mental state. The efficacy of the treatment is analyzed.
- Improved compliance with defined treatment schemes.
- Enter extensive information to the patient and his family[28].

It is recommended to commence antidepressant therapy and to sustain this regimen during the acute phase, generally lasting four to eight weeks. This method seeks to expedite the achievement of remission during an acute depressive episode. It is recommended to commence treatment with antidepressants and to sustain this regimen during the acute phase, generally lasting four to eight weeks. This method seeks to expedite the achievement of remission during an acute depressive episode. The treatment duration is 4 to 5 months. This phase is referred to as the continuation stage and aims to preserve a patient's remission status. Upon concluding this ongoing period, which lasts a minimum of six months from the initiation of therapy, the physician will evaluate the patient's medical history to ascertain the necessity of maintaining the antidepressant regimen to avert a return of the depressive episode[28].

Factors to consider for a specific antidepressant treatment:

Patient demographics: Half-life denotes the duration necessary for fifty percent of a substance to be metabolised by an organism. In the financial context of different categories of antidepressants, it should have been utilised earlier to examine the fourth evaluation of prior responses to antidepressants.

A comparative analysis was done to evaluate the efficacy of each antidepressant medications. Reflections on security, tolerance, and possible adverse effects. The coexistence of concurrent mental and systemic disorders.

Evaluate the potential for drug interactions with concomitant drugs that patients may utilise prior to commencing antidepressant therapy. Persistence of symptoms and reaction to therapeutic measures.

Evaluation of hazards to others, including the potential for self-harm. The quality of life.

The manifestation of any adverse effects associated with treatment.

Patient Consultation

To assess treatment efficacy and guarantee patient safety, persons receiving psychotherapy undertake regular monitoring. In Denmark, 55% of persons diagnosed with serious depression received treatment with antidepressants, either alone or alongside psychotherapy (nearly15%), while a significant 30% were receiving psychotherapy entirely for their treatment. Individual patient factors, such as symptom severity, therapeutic goals, treatment type, social support availability, and adherence to the treatment regimen, are considered when establishing the frequency of patient visits (29).

Pharmacological intervention for major depressive disorders

The primitive group of recognised antidepressants medication were the 5-HT & NA reuptake inhibitor, TCA like imipramine , and the MAO inhibitors like iproniazid. The amalgamation of these anti-depressants and electro-convulsive therapy has significantly reported to contribute to a therapeutics system that has led to a marked decrease in the population of depressed patients in psychiatric institutions[30]. Subsequent to the finding of these fundamental medicines, other compounds demonstrating similar mechanisms of action have been synthesised, leading to considerable progress in the enhancement of antidepressant therapy. Initially, irreversible monoamine oxidase inhibitors that obstructed the activities of both monoamine oxidase A and B isoforms were utilised. Subsequently, these were replaced with selectively irreversible drugs, such as the monoamine oxidase A inhibitor clorgyline and the monoamine oxidase B inhibitor selegiline. Ultimately, these medications were supplanted by the reversible monoamine oxidase inhibitor moclobemide. In conjunction with these breakthroughs in pharmacological treatment, notable progress has been achieved in the field of monoamine

reuptake inhibitors. Tricyclic antidepressants, such as imipramine and amitriptyline, function by obstructing the reuptake of noradrenaline and serotonin, while concurrently acting as antagonists of alpha-1, histamine-1, and muscarinic receptors, and were previously the primary therapeutic options. Nevertheless, they have predominantly been replaced by more selective pharmaceuticals that present a diminished occurrence of adverse effects. The pharmaceutical drugs under consideration comprise SSRIs, like fluoxetine, and SNRIs, such as venlafaxine[30].

Pharmacotherapies

Antidepressants drugsare recommended as the main stayoftreatment option for people with mild to moderate inmajorityof depressants. Antidepressant choice is based on patient safety and ability to withstand anticipated side effects. Pharmacological features including halflife, interactions between medicinal products, and effects on cytochrome P450 enzymes are meticulously assessed to adapt to patient needs. Among other things, considerations include patient preferences and costs. SSRIs, SNRIs, bupropion and mintazapine are generally preferred over TCAs. The efficacy and use of treatment efficacy and side effects, including gastrointestinal symptoms, sedation, insomnia, activation, weight variation, cardiovascular, neurological, anticholinergic or sexual side effects, are systematically observed to protect well-being in patients[31].

Pharmacodynamics of antidepressant drugs

The mono-amine hypothesis of the depression asserts that a single mechanism governs both the physiological aspects of depression and the effectiveness of antidepressant treatments. This theory suggests that depression results from reduced activity in serotonin and/or norepinephrine, which is subsequently normalised by the use of antidepressants drugs. Research supporting this notion has consistently shown that the depletion of monoamines in patients underscores the critical necessity of functional monoaminergic pathways in combating depression; all current treatments aim to restore compromised monoamine function. Mono-amines have been linked to the aetiology of depression, as indicated by the antidepressant -effects exhibited by hydrazine derivatives such as iproniazid. Irreversible MAOIs operate by obstructing the enzymes responsible for the degradation of monoamines. Although these enzymes exhibit effectiveness, their

tolerance is diminished by related side effects; hence, reversible monoamine oxidase inhibitors are preferred for their enhanced safety profiles and tolerability. Extensive discussion has arisen around the exact method by which antidepressants affect monoamines. Nonetheless, studies on neurotransmitter depletion have offered compelling evidence that the mechanism of antidepressants corresponds with the augmentation of 5HT and NA neurotransmission. Although different kinds of antidepressants function via various methods, they nonetheless possess numerous common traits. The primary mechanism entails the interaction of all antidepressants with monoamine systems, specifically via their engagement with catabolic enzymes, receptors, or transporters that mediate monoamine reuptake. Moreover, all antidepressants operate as multi-target drugs by engaging with diverse receptors to increase monoamine levels. Tricyclic antidepressants such as imipramine and amitriptyline operate by obstructing the reabsorption of norepinephrine and serotonin. Nonetheless, their extensive target profiles result in the antagonism of α1adrenoceptors, muscarinic receptors, and histaminergic receptors basically H-1, as well as influencing cardiac ion channels. The multi-target action inherent in the TCA group of antidepressants accounts for their suboptimal tolerability profile. The class of antidepressant medications known as SSRIs is presently regarded as the most secure option. While this category does exhibit a range of side effects, it has demonstrated superior tolerability compared to TCAs and MAOIs. SSRIs provide improved security profiles, but their effectiveness does not exceed TCA. Nevertheless, they continue to be preferred options for the treatment of long-term depressive diseases. The selectivity of SSRIs was exposed to factors that reduced their effectiveness. This hypothesis influenced the creation of venlafaxine, serotonin, and SNRIs. Due to their rapid activity, SNRIs are more effective than SSRIs, but share similar side effects with SSRIs. The administration of antidepressants typically necessitates a latency period of 3-4 weeks before achieving therapeutic efficacy, a phenomenon that appears to be inescapable. Furthermore, there remains considerable discourse regarding the potential of these pharmacological agents to deliver rapid yet enduring alleviation from depressive symptoms. Although antidepressants rapidly elevate extracellular monoamine levels, the lag in their therapeutic benefits is ascribed to the initiation of neuroplastic processes. These phenomena may include neurogenesis, changes in neuronal anatomy, variations in

receptor density & intra-cellular signalling, as well as shifts in synaptic transmission and their architecture. Transcription factors, including cAMP-responsive-element-bindingprotein, immediate early genes such as the Arc, neurotrophins like the BDNF, and antiapoptotic proteins such as the bcl-2, function as mediators linked to the ability of antidepressants drugs to promote neuronal proliferation and resilience. They also contribute in mitigating the changes caused by chronic stress and excessive cortisol release[47]. The importance of neuronal plasticity and cellular models of G protein/receptor binding were determined as critical factors in characterizing novel antidepressants. Existing limitations with SSRI/SNRI therapy are based on an inadequate understanding of the pathophysiology of major depression, perhaps as with other psychiatric symptoms[32]. All antidepressants need at least two weeks for observable improvements to be apparent. In certain cases, the period can be extended up to 8 weeks. Clinical treatment effects require time to show their benefits, but side effects can be experienced immediately[32].

Frequently used antidepressants Fluoxetine and Citalopram

Fluoxetine is a SSRI commonly indicated for the treatment of depression, OCD(obsessive-compulsive disorders), and the bulimia nervosa. It is additionally indicated for the anxiety disorders too, especially generalised anxiety-disorders, as well as anxiety and impulse control disorders. Fluoxetine is the preferred selective serotonin reuptake inhibitor when indicated for children or adolescents. Its application necessitates careful consideration in older individuals, those with liver or kidney dysfunction, and patients with diabetes. Research indicates that older patients exhibit a heightened vulnerability to CNS adverse effects, including agitation, nervousness, and excessive sedation. Fluoxetine has demonstrated efficacy in treating depression in paediatric patients as well starting from the age of seven years [33].

It is essential to use caution while administering these drugs to paediatric populations, as all antidepressants provide an increased risk of suicidal thoughts in group of pediatric population. Fluoxetine should be prescribed with caution in pregnant individuals too due to the possible risk of the premature delivery. When we used in conjunction with the other serotonergic related medications, it has been shown to increase the risk of serotonin-syndrome, that is characterised by fever, restlessness, agitation, rigidity, and gastro-

intestinal (GI) symptoms. The common side effects include encompass nausea, weight gain, increased hunger, disorientation, chest pain, palpitations, and hypertension. A key difference between the fluoxetine and the citalopram is that fluoxetine has got a longer half-life of three extradays, whereas citalopram has a lower propensity for drug interactions. Fluoxetine inhibits the enzyme CYP-2D6, making it prone to numerous medication interactions, unlike citalopram. Therapeutic drug monitoring is crucial for specific drugs used concurrently with fluoxetine, such as diazepam, warfarin, lithium, and carbamazepine, a sodium channel blocker. Citalopram is favoured over amitriptyline due to its enhanced safety profile among these patients. These group has negligible anticholinergic effects and exhibits less cardiotoxicity too. Its half-life is significantly less than that of fluoxetine, which is of total36 hours. Citalopram acts as a mild inhibitor of cytochrome P-450, leading to a diminished likelihood of medication and other interactions (drug-drug or drug-food). The S-enantiomer of the citalopram is known as es-citalopram, a one of the frequently prescribed in managing patient of depression as antidepressant drugs[34].

Venlafaxine

Venlafaxine functions as a SNRI and additionally exhibits properties as like weak dopamine re-uptake inhibitors. This medication is primarily utilised in the management of major depressive episodes and the generalised anxiety disorders (GAD). The use of this treatment in pediatrics is generally discouraged, primarily due to the lack of established risk-to-benefit ratios for individuals under the age of 18. The predominant side effects are primarily of a central nervous system origin, encompassing headache, insomnia, dizziness, nervousness, visual disturbances, and the somnolence. The drugVenlafaxine has been observed to induce GI-gastrointestinal effects, including dry-mouth, constipation, nausea, vomiting and, anorexia,. It has also been demonstrated to induce the sexual dysfunction, a adverse-side effect that has been found to diminish patient adherence. The cardiovascular-CV side effects include hypertension, postural hypotension, palpitations, and some time tachycardia. The sexual dys-function induced by venlafaxine frequently correlates with their diminished adherence chances[35].

Factors associated to antidepressant efficacy

Genetic variables significantly influence the clinical response to antidepressant medications, which is then reflected in the behavioural changes observed by physicians

as progress. These are the genetic factors introduce further complexity to the already intricate neuro-biological components influencing the clinical- response to SSRIs and the SNRIs.

Polysmorphisms in the promoter region of the transporter like SERT were identified as determinants of susceptibility to primary depression and the efficacy of antidepressant therapy. Improved response to SSRI was associated with heterozygotes and long variational homozygotes compared to shorter versions of homozygotes. Individual nucleotide polymorphisms in serotonin-related genes, including serum and tryptophan hydroxylase 1, have been shown to correlate with responses to antidepressants. Increased activity and expression of 5-HT1A receptors due to G(1019) polymorphisms in the promoter region are correlated with depression, suboptimal antidepressants, and increased risk of suicide. Similarly, genes involved in catecholamines were associated with responses to antidepressants. Phosphodiesterase genes involved in the amine signaling pathway and polymorphism of the KCNK-2 gene are often belongs with increased sensitivity to primary depressions and antidepressants' efficacy and treatment resistance. A large number of SNPs were found in the BDNF gene, one of which has been linked to severe depression and response to antidepressants. Polymorphisms in the glucocorticoid receptor-FKBP5 were associated with responses to antidepressants and recurrence of depressive episodes. Polymorphisms associated with inflammatory genes were identified as correlated with depression and susceptibility to treatment response. As expected, clinical responses to SNRIS and SSRIs are affected by genes that do not contain monoaminergic neurotransmission. Polymorphisms in ABCB1, which play a role in drug transport through the blood-brain barrier, affect brain concentrations of antidepressants, and thus influence the treatment response. In 2008, Irving Kirsch and colleagues published a meta-analysis showing that most patients were not significant for most patients. Despite improved compliance, the new drug did not exceed the effectiveness of certain tricyclic antidepressants, including clomipramine. He asserted that their data reveals a minor advantage of the medicine over placebo, which is statistically significant solely for major depressive illness, but has no effect on moderate depression. The meta-analysis results indicated that individuals with mild depression who received a placebo exhibited recovery rates comparable to those of patients administered their medicine for their treatments.[36] This raised doubts about the effectiveness of antidepressants, which

have been used almost 50 years before this metaanalysis was published. Based on the results of the meta-analysis, a researcher specialised in neurobilogy naming Kirsch found that SSRIs do not offer any advantage over the placebo group. Antidepressants do not affect the long-term outcome of depression and the risk of suicide, and existing guidelines for risk-treating antidepressant recipes should be reassessed in the area of antidirectives by dealing with risk. Typical antidepressants, including SSRIS and TCAS, are used. Conversely, naturalistic studies (star*D) such as sequenced treatment alternatives to depression show less favorable results in 30% and 50% remission and 50% remission and 50% remission after treatment with citalopram[34]. Actual patient results show that a significant proportion of diagnosed depression and that standard anti-statement therapy is only partially responsive. As a result, these patients should require further treatment with alternative interventions such as lithium, atypical antipsychotics, or electro conductive electrotherapy. A significant limitation of antidepressants is the delayed onset of treatment effectiveness on patients. This often generates skepticism compared to patient effectiveness, leading to reduced patient compliance. The above effects are usually observed at 6-8 week intervals, with antidepressants indicating the distinction between placebo treatments. Conversely, it was demonstrated that 39% of patients reached remission after 8 weeks of antidepressant treatment (easiness of 1.10 on the Hamilton rating scale for depression, or Montgomery's assessment of depression. Another one study showed that all the antidepressants exceeded placebogroup, regardless of outcome measures used. Compared to placebo, TCAs are extremely effective in short-term treatment of severe depression. Compared to placebo, antidepressants showed significant effects on moderate and severe depression. The effectiveness of antidepressants on depression is clear, but considerable attention must be paid to the risk-benefit ratio associated with use. Antidepressants often form the risk of the side effects such as nausea, sedation, indifference, fatigue, weight gain, sexual dysfunction, and therapeutic benefits. The etiology of depression has been investigated for decades. The cause is often associated with chemical abnormalities in the brain. The diagnosis of depression is determined according to the specific criteria listed in the DSMV manual. Treatment of depression is based not only on antidepressants, but also on treatment meetings with psychiatrists[36,37].

Medications for depression have been produced after extensive study aimed at discovering innovative treatment methods for the disorder. Various classes exhibit distinct mechanisms of action. The three primary classes utilised are TCAs. SSRIs, and SNRIs.

Review of utilisation of antidepressant drugs

Retrospective assessments use existing data collected for other purposes, primarily as studies presented by regulations and patient files. Retrospective assessments help identify prescription patterns, hand over or administer medications, prevent inappropriate medication consumption, and form the basis for the development of future recommendations and targeted interventions. This DUR involves analysing patient medical records to ascertain if the drug therapy complies with the 3 C 2.1 standards. Retrospective drug utilisation studies establish accepted criteria that assist prescribers in enhancing care for individual patients and certain patient groups, including individuals with psychiatric problems.

An important factor that must be evaluated during a retrospective assessment is the amount of drug delivered, which is compared to the appropriate dosage. Antidepressants should be administered in appropriate doses to achieve intended treatment outcomes and prevent toxicity. The DDD approach (defined daily dose) is a drug use study used for data analysis. DDD refers to a dose that represents the average dose of a drug when used for the primary indications of adults. There are restrictions on DDD. This is because a significant proportion of drug therapy for off-label applications is used, leading to different doses. A DDD is a technical measurement unit that does not necessarily correspond to the average amount actually provided. Dose instructions indicate daily frequency of drug debt and facilitate calculation of the overall daily dosage. A related expression of this methodology was a study conducted in 2000, in which we examined a sample of 98 young people and young people from South Africa and analyzed prescribing patterns for TCA and SSRI. This indicates that SSRIs are specified more frequently in the proximity of DDDs. The study of Bauer and colleagues sought to educate prescribing patterns and factors that influence antidepressant drug selection within factors affecting the study of depression (FODER), including 3,468 patients in 12 EU- European countries. This study was conducted on the basis of growing interest among European researchers after voting through differences in antidepressant prescriptions in European

countries, with TCA being preferred in some countries and SSRIs[55]. Despite other studies, this difference has been observed, indicating a transition from TCA prescription to more acceptable SSRIs. F-I-N-D-E-R was an observational study conducted in 12 major countries: UK,

Germany, France, Austria, Belgium, Ireland, Italy, Netherlands, Norway, Portugal, Sweden, and the Switzerland . This study was conducted to clarify factors that influence the HRQOL-(health related quality of life), outcomes in patients treated for depression. This study was used by researchers to identify physician and patient factors that influence initial selection of antidepressants. All participants in this study were people over the age of 18 years. The results of this study showed that the most frequently prescribed antidepressant was SSRIS, caring for 63.3% of all patients followed by SNRIS in 13.6% of all patients[58]. The prescription rates for the various antidepressants were different. SSRI was prescribed at a rate of 32% in Germany and 82% in France state. TCAs were prescribed only 1.5% of patients in the Netherlands and 8.6% only in Austria, in contrast 26.5% of antidepressants prescribed in Germany. In Austria, antidepressant combinations were administered more frequently for 24.5% of patients, but in the Netherlands and Ireland the combination was not used. The average dose of amitriptyline (55.6 mg/day) is well below the recommended dose (75 mg/day). In particular, it was shown that GPs are prescribing larger media doses of amitriptyline and venlafaxine with budget doses of duloxetine and trazodone. This study used Medicaid program data with descriptive time series to assess trends in terms of cost, use, market shares and price for SSRIs, TCAS, and other antidepressants. Research showed that antidepressants were the most common prescription in the United States in the 1990s. The survey showed a significant increase in antidepressant prescriptions from 6.8 million in 1991 to 35.0 million in 2004, and a decrease of 32.7 million in 2005. The dominance of SSRI recipes was accounted for by an increase in recipes from 10 million in 1991 to 20.8 million in 2005 (59). TCA recipes have always increased from 4.7 million in 1991 to 6.4 million in 2001. It then showed a small cut in 2002, and in 2005 it fell sharply to 3.7 million people. The increase in overall use of antidepressants in the aging population group increased from 3.9% in 1991 to 8.3% in 2011 (60). This study showed variability in prescribing TCA. Amitriptyline and the paroxetine were the most frequently prescribed antidepressants, and mirtazapine and the venlafaxine were also not prescribed to a lesser extent (60). The study examines the

increased use of SSRIs in the demographics of older adults and middle geriatric people, perhaps low toxicity, benign and unfavorable drug reactions, and the lack of need for plasma monitoring[61]. The comparatively stable prevalence and minor reduction in the utilisation of TCAs were found to align with existing literature[61], despite researchers anticipating a more significant decline in their usage owing to poor tolerability and their status as a non-preferred antidepressant among the elderly population[60].

The increased prevalence of TCA use may be due to the various purposes for which these medications are prescribed, including neuropathic pain[62]. In addition to worsening chronic disease, increased antidepressant consumption in older adults can be attributed to increased loneliness, physical health issues, and other limitations[60]. A study conducted in Spain showed that the most frequently prescribed antidepressant was SSRI, earning 63.8%, followed by a TCA of 18.2% (63). A US-based study showed that 71% of patients received SSRIand/SNRI its Depressant, while only 3% received older antidepressants such as TCA. The number of TCAS recipes has consistently increased from 4.7 million to 6.4 million in 1991to 2001, followed by a slight decline of 600,000 in 2002 and a significant decline of 3.7 million in 2005. This finding was confirmed by additional research in several European countries. In the Netherlands, TCA was given only 1.5% of patients, and in Austria the number was 8.6%. Conversely, they accounted for nearly 27% of antidepressants prescribed in Germany. The dominance of SSRI recipes was accounted for by an increase in recipes from 10 million in 1991 to 20.8 million in 2005. Of the nearly 17000 antidepressants prescribed, 42% were the SSRIs and 5,739 (34%) TCAS (63). In South Africa region, previous trials showed a comparable trend that showed that the most frequently prescribed antidepressant TCAs constituted 40.9% of all antidepressant recipes followed by selective serotonin RE absorption. Prescription trends for TCAs were analyzed using patient data recorded in private medical assistance programs, particularly from 1996 (1982 patients) and 2003 (2345 patients. Approximately twothirds of these patients were women (67% in 1996 and 58% in 2002/2003). Surprisingly, TCA was often awarded to men in 1996 than to women in the course of younger ages, while the same trend was observed in older cohorts in 2002/2003. Despite continuing debate over the efficacy of SSRIs compared to TCA and other older antidepressants, the consensus between health profession psychiatrists and relatives is that SSRIs should be the preferred early pharmacological treatment due to their relatively

mild side-effect profile. An early Danish drug consumption analysis showed that around 75% of patients were prescribed TCAs, while SSRIs used only 10% of the population (38,39,40). This illustrates the development of antidepressant use over the years[63].

MATERIALS & METHODS

Chapter 4

MATERIALS & METHODS

This study was performed in the department of Psychiatry and Pharmacology, Santosh Medical College & Hospital, a tertiary care hospital Santosh University, Ghaziabad, India.

4.1 Ethical consideration:

Ethical approval of the study was granted prior to the study from the IEC (institutional ethics committee) of the Santosh University (F. No.SU/R/2023/2489[28]. Ethical clearance certificate is attached with the annexure. All study population was conveyed about the purpose and objectives of the study. A written informed consent was procured from each participant or their legal representative for the interview and other data analysis of their prescriptions. They have given full authority to refuse their inclusion during the course of study, without affecting their hospital services. Patients were also ensured about their privacy and confidentiality of the demographic profile, disease or treatment characteristics were fully maintained. All the information regarding patients gathered were used only for the assessment of epidemiological pattern in concern department.

Study design: Hospital based Observational study

Sample size: 217. The sample size of this study was calculated by using the proportion formulae.

Method of subject selection: Constant enumeration

It was an observational; prospective study (hospital based), it has been conducted over a period of one year. (October-2023 to November-2024).

4.2 Criteria of patient inclusion & exclusion

Inclusion criterias:

Patients who have visited psychiatry OPD and diagnosed with any psychiatric disease by the specialist of psychiatric department.

- Patients who have prescribed at least one medication for the treatment or control of mental illness.
- Taking treatment for the first time for the depressive illness.
- At least 18- years of age on the day of OPD visits.
- Patients or his/her legal representative ready to give informed consent of the study.

Exclusion criteria:

- Patients presented with prescription errors, accidental and deliberate over dosage.
- Patients or his/her wards not able to convey the detail of ADRs or DRPs occurred following psychiatric drug usage.
- **Patients' prescription was analysed in the study that not fulfilled the inclusion criteria.**

4.3 Data collection

Data collection was done using specialized performa to study the demographic profile of the patients, Depressive disorder diagnosed, Antidepressant drugs used were obtained from the patient prescription or his/her legal guardian. Safety of prescribed drugs by evaluating DRPs & ADRs and adherence to treatment guideline were assessed by observation or interviewing the patients or his/her wards. Details of the comorbidities and concomitant drugs prescribed by the specialist of psychiatric department with relevant test reports were noted. Management of DRPs by the treating physicians was also noted.

4.4 Study protocol

All mental disorders presented in the psychiatry department were diagnosed in accordance to the ICD-10 System of WHO classification of Depressive illness.

Prescribing pattern of antidepressant drugs were analysed using WHO core indicators, details of the recommendation given below:[41]

Patient care indicators

1. The WHO recommends a figure of 1.6–1.8 for the average number of drug

prescribed per prescription, which is computed by dividing the total number of prescriptions by the number of total prescriptions surveyed.

2. The percentage of encounters with antibiotics is computed by multiplying the total number of surveyed interactions by 100 and dividing the number of encounters where an antibiotics was prescribed (WHO suggested values: 20 to 26.8%).
3. The percentage of encounters with the use of an injection is determined by multiplying the total number of surveyed interactions by 100 and dividing the number of encounters where an injection was prescribed (WHO suggested value: 13.4-24.1%).
4. The percentage of prescriptions written under a generic name is determined by dividing the total number of prescriptions written under a generic name by 100 (the WHO suggested value is 100%).
5. The percentage of prescription drugs that come from the essential medicine list (EML) is determined by multiplying the total number of prescription drugs by 100 (the WHO suggested value of 100%) and dividing the number of prescription drugs that are in the Essential medicine list-ML.

Prescribing Indicators

1. The percentage of prescription drugs that are actually filled is determined by dividing the, total number of prescription drugs by the number of total prescriptions filled, then multiplying the result by 100 (the WHO suggested value is 100%). A prescription was deemed filled if the pharmacy filled the generic drug, even if a different brand was used in place of the one that was prescribed.
2. Relative to the total number of medications issued, the percentage of medications that are genuinely labelled is determined by dividing the number of medications by 100 (the WHO suggested value is 100%).

Analysis of severity of depressive symptoms

Studies of HAM-D & MADRS score were done to identify the severity of depressive symptoms at the time of admission & on 6 weeks follow up,

Zimmerman et al. study of 2013 imply that a HAM-D score of value (**8–16**) reflects mild symptomatology, but a score of value above 17 and up to 23 denotes moderate severity of depression. A score of 24 indicates a serious depressive episode (11, 41).

The MADRS is a 10-item scale (range: 0–60) utilised to assess depressive symptom scores over the preceding week, including factors such as reported sadness and inner tension[42]. Prior research has suggested the subsequent severity estimates according to the MADRS score: The MADRS is a 10-item scale (range: 0–60) utilised to assess depressive symptom scores over the preceding week, including factors such as reported sadness and inner tension[42]. Prior research has suggested the following severity classifications according to the MADRS score: (I) 0 to 6 indicates no depression; (II) 7 to 19 signifies mild-depression; (III) 20 to 34 reflects moderate-depression; and (IV) scores above 34 denote severe -depression[43].

Safety of prescribed drugs

For the safety of the prescribed drugs, ADRs produced by them were studied using the definition of WHO-ADR in this study (44). The Central Drugs Standard Control Organization's (CDSCO) suspected ADR reporting form was used to document the discovered ADRs.

Cost-effectiveness study of antibiotic used

The mean price value per tablet was found in-order to determining the direct costs of medications in-accordance with the WHO CHOICE recommendations. The mean price value (MPV) was noted in rupees (INR). The average of the cost per-patient each day were determined.

4.5 Statistical tests and data analysis

In this study, data analysis was done using SPSS, version- 25) software, Inc, USA. A number of statistical software is available for the analysis, however, it is the most popular and extensively used software for analyzing data in epidemiological studies [45]. Patient's demographic characteristics and their treatment profile were studied by using descriptive statistics for the frequency, proportion and distribution.

HAM-D & MADR severity study have been performed in order to find any association with triggering factors by using Pearson chi square statistics.

Frequencies of ADRs, pattern of usage of drugs by WHO core indicators was performed. For evaluation of association of socio-demographic variables and usage pattern, Pearson Chi-square statistical test was used in the study.

The Chi-square test of independence used in our study, often known as the Pearson Chisquare test, is one of the best statistics for assessing the hypotheses when the variables are nominal, as they usually are in clinical research. The Chi-square test, in contrast to other statistics, may give exact information about the significance of any differences that are seen as well as which categories are responsible for any differences that are found. In the end, the quantity and caliber of data this statistic offers make it one of the most crucial instruments in a researcher's toolkit for analysis[46].

The 95% confidence interval was used to evaluate the statistical significance. P values considered ($p \leq 0.05$) were deemed statistically significant in the investigation of risk factor associations.

RESULTS

Chapter 5

RESULTS

Social & Demographic pattern of the participants

A total of 217 prescription samples were collected to analyse in the study. The mean age of the total patient participated in the study was 40.39 (Standard Deviation- 5.96), minimum age was found out to be 27 years and maximum age was 58 years in this study. Out of 217 patients, 110 patients were females and more than half of the patients (53.46%) were single when visited the psychiatry department. In this study a total of 24.32% patient of psychiatry was presented with comorbidities majorly with hypertension (13.82%) followed by migraine (7.37%), Parkinson's disease (1.84%) and epilepsy (1.38%). A total of only 2.3 percent patients of study participant received combination of drugs in term of antidepressant medication. Majority of the prescriptions were of mono-therapy at a time.

In this study participant were noted from rural as well as urban areas in a very similar fashion. While 61.75 percent of the total population recorded as unemployed at the time of hospital visit. Majority of the participant lie in lower income group (65.44%) followed by medium (25.35%) and high (9.22%). In total of 217 patient 14.29 percent were reported as alcoholic and 10.14 percent were smokers, apart from this 18 percent of them reported to have family history of psychiatric disorders (Table1,2).

Treatment pattern of the patients attended psychiatry department

In this study 33 percent of the patients received Fluoxetine as antidepressant drug, while 32 percent prescription was containing citalopram as main medication. Other medication used in this study was amitriptyline (11%), imipramine (6%), escitalopram (5.5%), sertraline (5.5%), paroxetine (5%) and combination drugs like clonazepam with fluoxetine (2%).

ADRs pattern of the prescribed drugs

Out of 217 participants, 216 had at least one ADR identified, Table 3 provides information on the incidence of ADRs. Top on the list of most frequent ADRs are cases of headache, dizziness, dryness of mouth, insomnia, weight gain, sexual dysfunction, diarrhea and others. Details of the drug causing ADRs depicted in figure 2,

Table 1: Sociodemographic characteristics of the participant attended psychiatry department (*n*=217)

VARIABLES	Frequency (%)
Age (years)	Mean (40.39)
Sex	
Female	110 (50.69)
Male	107 (49.31)
Marital status	
Single	116 (53.46)
With partner	101 (46.54)
Professional status	
Employed	83 (38.25)
Un-employed	134 (61.75)
Income status	
Low	142 (65.44)
Medium	55 (25.35)
High	20 (9.22)
Social habit	
Alcoholic	31 (14.29)
Smoker	22 (10.14)

Table 2: Clinical characteristics of the patients attended psychiatry department (*n*=217)

VARIABLES	**Frequency**	**Percentage (%)**
Presence of Co-morbidities		
Yes	53	24.32
No	164	75.68
Comorbidities		

Hypertension Migraine Parkinson Disease Epilepsy	30 16 4 3	13.82 7.37 1.84 1.38
Antidepressant therapy prescription		
Mono-therapy	212	97.97
Combination therapy	5	2.03
Routes of drug administration		
Oral	155	71.43
Injectable	58	26.73
NLEM		
Yes	130	60.6
No	85	39.4

Drug utilization pattern

Antidepressants drugs made up an average of 1.025 prescriptions. 2.3 percent of prescriptions for medications were FDCs. 10 percent of prescriptions for medication were written under a generic name. Approximately 60% of the antidepressant medications prescribed came from the list of NLEM. 27 percent of the total drugs used as parenteral form. (Table 5)

Usage pattern of antidepressant drugs

Most frequently used drugs was fluoxetine followed by citalopram, amitriptyline and others.

Table: 3 Antidepressant drug usage pattern of the patients attended psychiatry department (*n*=217)

Therapy	Frequency	Percentage
FLUOXETINE	71	32.72%
CITALOPRAM	70	32.26%

AMITRYP	23	10.6%
IMIPRAMINE	13	5.99%
ESCITALOPRAM	12	5.53%
SERTALINE	12	5.53%
PAROXETINE	11	5.07%
CLONAZEPAM + FLUOXETINE	5	2.3%
Total	217	100%

Table 4: Gender wise distribution of HAM-D & MADR Score of severity of depression in patients attended psychiatry department (*n*=217)

Severity Score		**Frequency**	**Percentage**	**Mean ± Std.**
HAM-D	F	110	50.69%	19.75 ± 4.13
	M	107	49.31%	19.9 ± 4.77
MADR	F	110	50.69%	26.12 ± 5.22
	M	107	49.31%	24.05 ± 5.84
HAM-D 6 wk	F	110	50.69%	9.68 ± 2.13
	M	107	49.31%	9.79 ± 1.74
MADR 6 wks	F	110	50.69%	10.92 ± 3.24
	M	107	49.31%	10.87 ± 2.9

Table: 5 Adverse effects produced by Antidepressant drug used in the patients attended psychiatry department (*n*=217)

Adverse effects	Frequency	Percentage
HEADACHE, DIZZINESS	57	26.27%
DRYNESS OF MOUTH	22	10.14%
CONSTIPATION	21	9.68%
INSOMNIA, WEIGHT GAIN, ABNORMAL DREAM	20	9.22%
SEXUAL DYSFUNCTION	19	8.76%
INSOMNIA, WEIGHT GAIN, ABNORMAL DREAM, HEADACHE	14	6.45%
INSOMNIA, HEADACHE ABNORMAL DREAM	13	5.99%
NAUSEA, HEADACHE	13	5.99%
DIARRHEA	12	5.53%
DIZZINESS	8	3.69%
HEADACHE, DIZZINESS, ABNORMAL DREAM	6	2.76%
SEDATION	5	2.3%
HEADACHE,	1	0.46%
HEADACHE, DIZZINESS,	1	0.46%
INSOMNIA, WEIGHT GAIN, CONSTIPATION	1	0.46%
NIL	1	0.46%
WEIGHT GAIN, CONSTIPATION	1	0.46%
INSOMNIA, WEIGHT GAIN	1	0.46%
WEIGHT GAIN, ABNORMAL DREAM	1	0.46%
Total	217	100%

Figure 1. Percentage of antidepressant drugs used in the study (*n*=217)

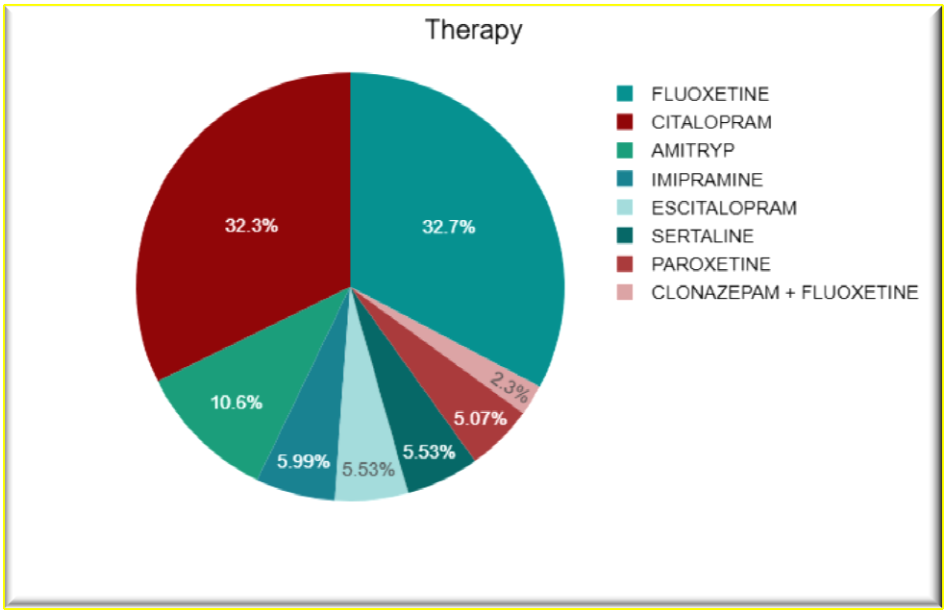


Figure 2: Depicting adverse effects by particular medication (*n*=217)

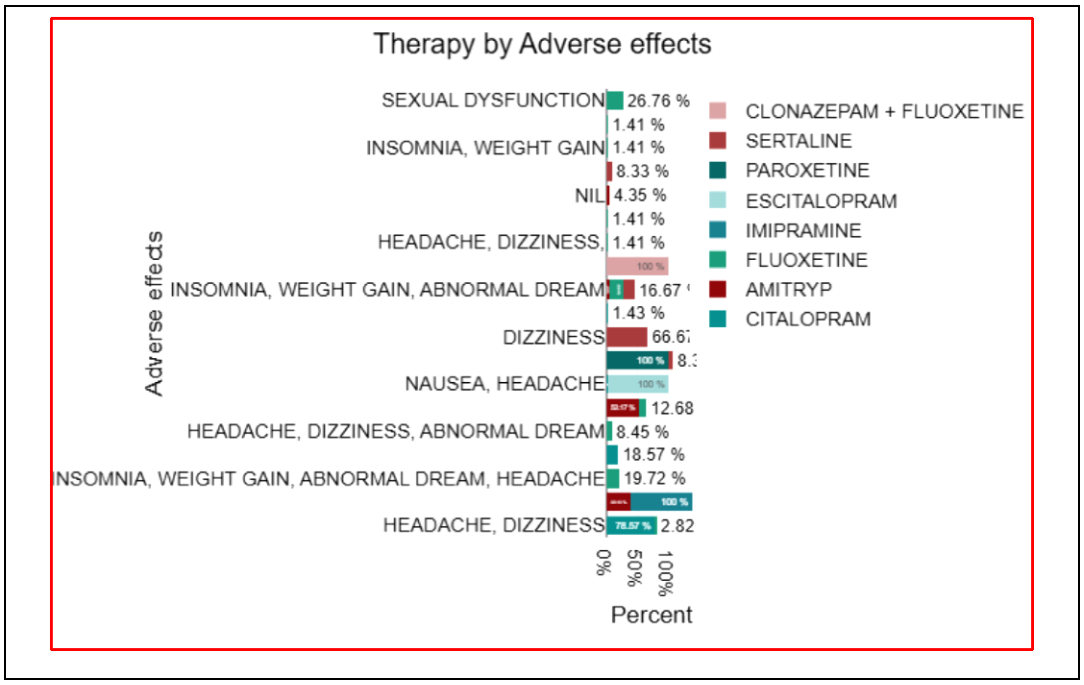


Figure 3: Percentage of antidepressant drug utilized according to NLEM 2022 (*n*=217)

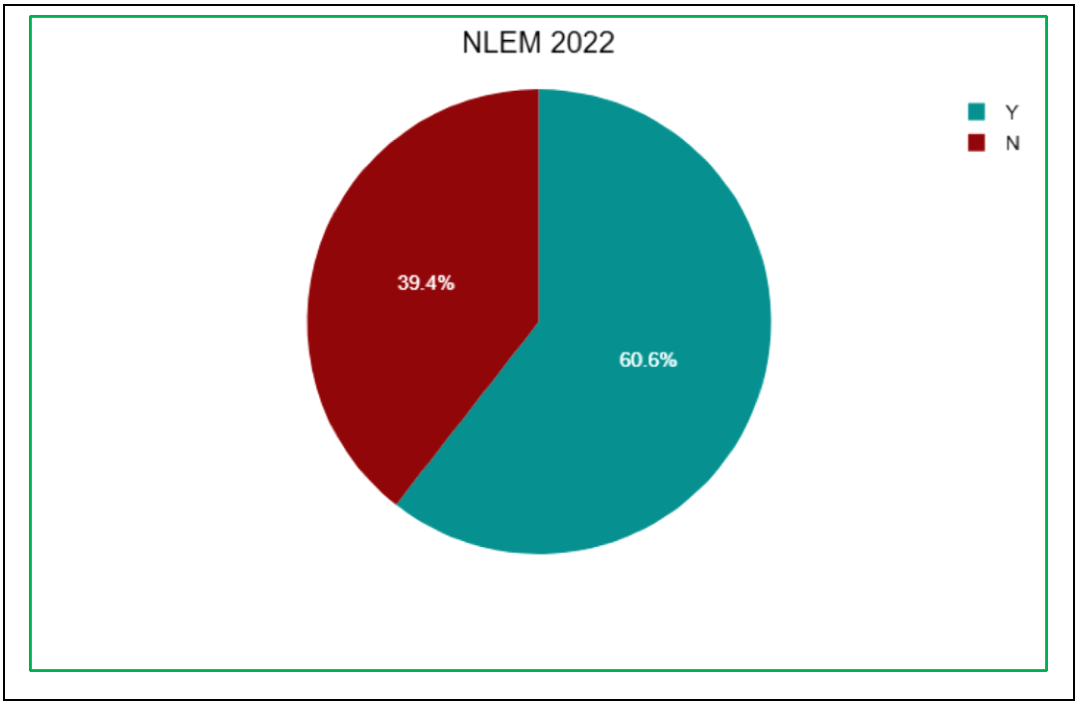
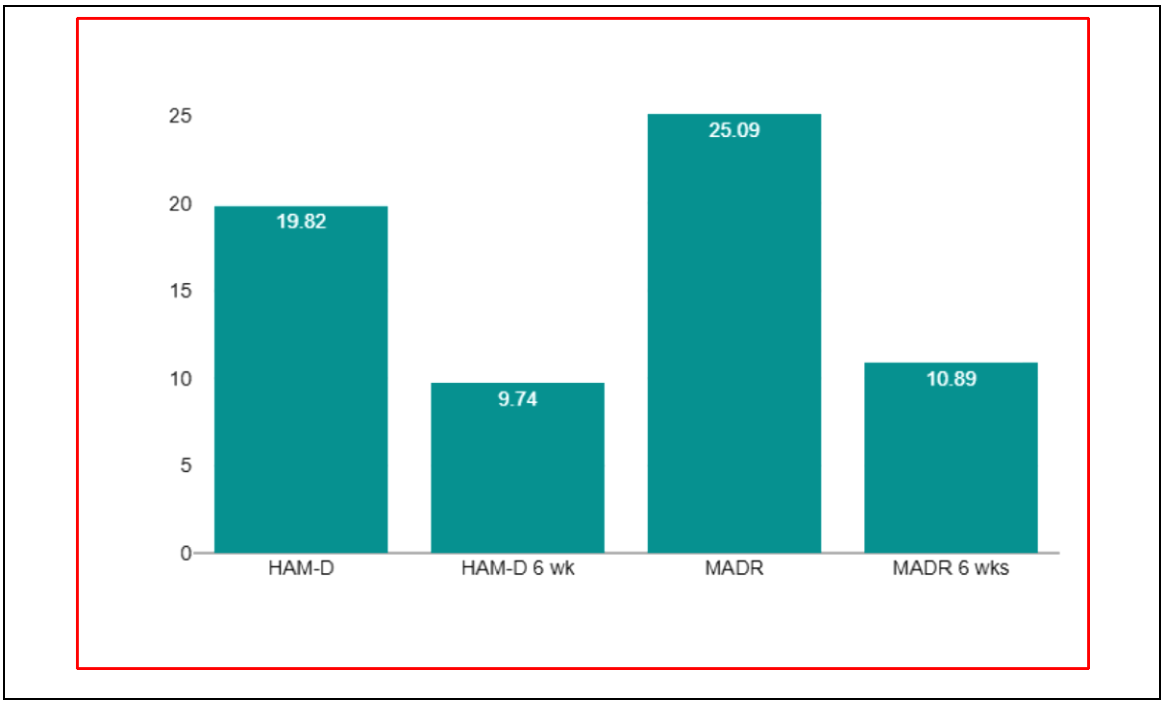


Figure 4: Depicting HAM-D and MADR score at admission & follow-up of 6 weeks of antidepressant treatment (*n*=217)

4.a



4.b

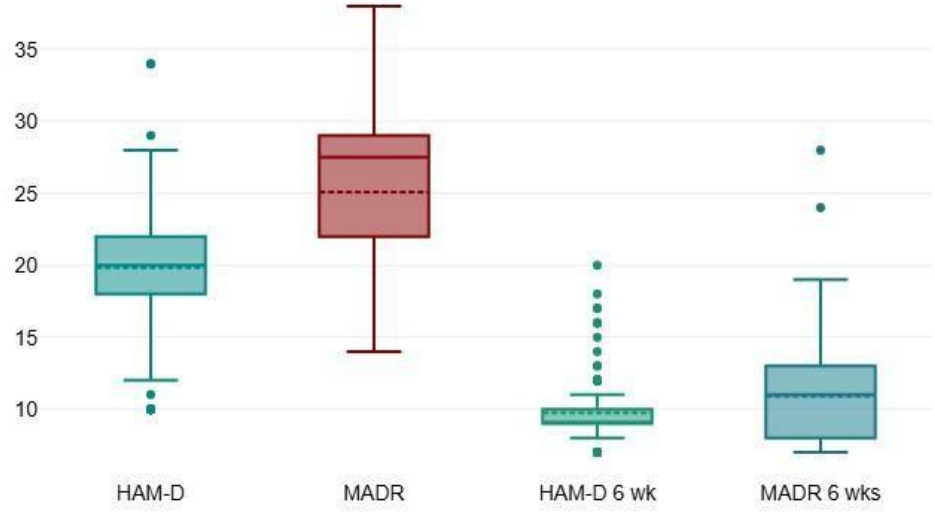
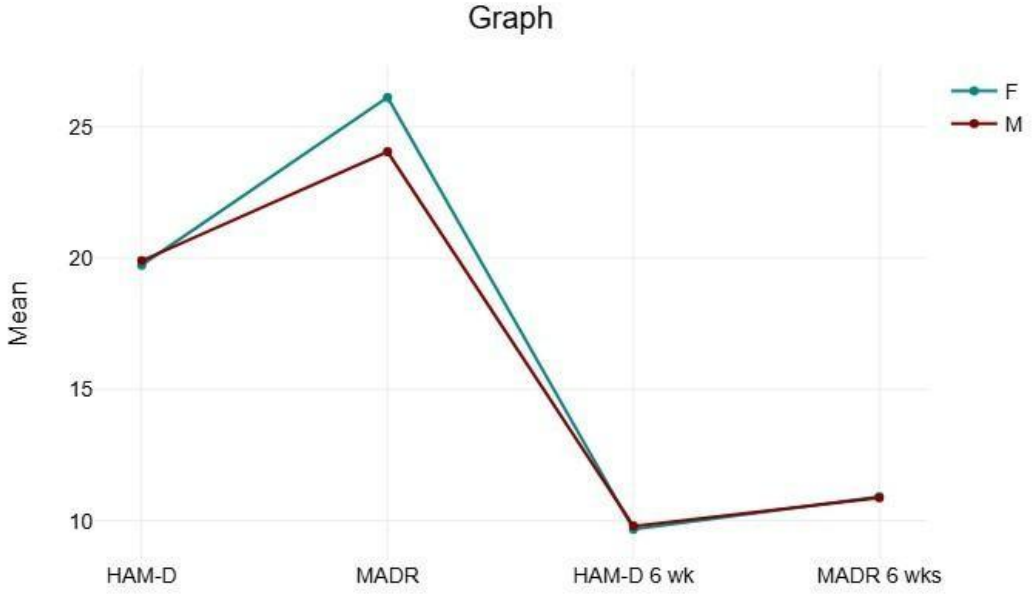


Figure 5: Decreasing pattern of HAM-D and MADR score at follow-up of 6 weeks of antidepressant treatment in male & female patients (*n*=217) 5a.



5.b

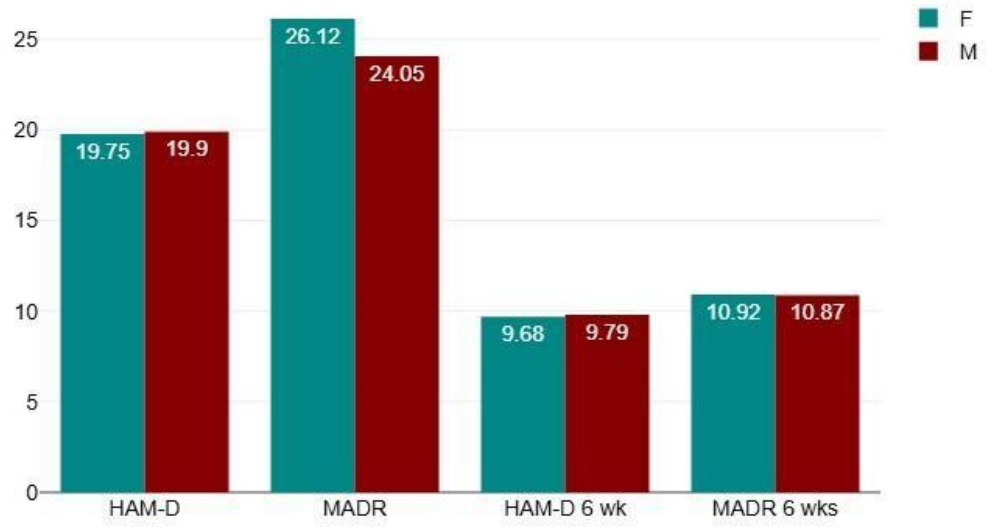


Figure 6: Decreasing pattern of HAM-D score at follow-up of 6 weeks of antidepressant treatment by particular antidepressant medications (*n*=217)

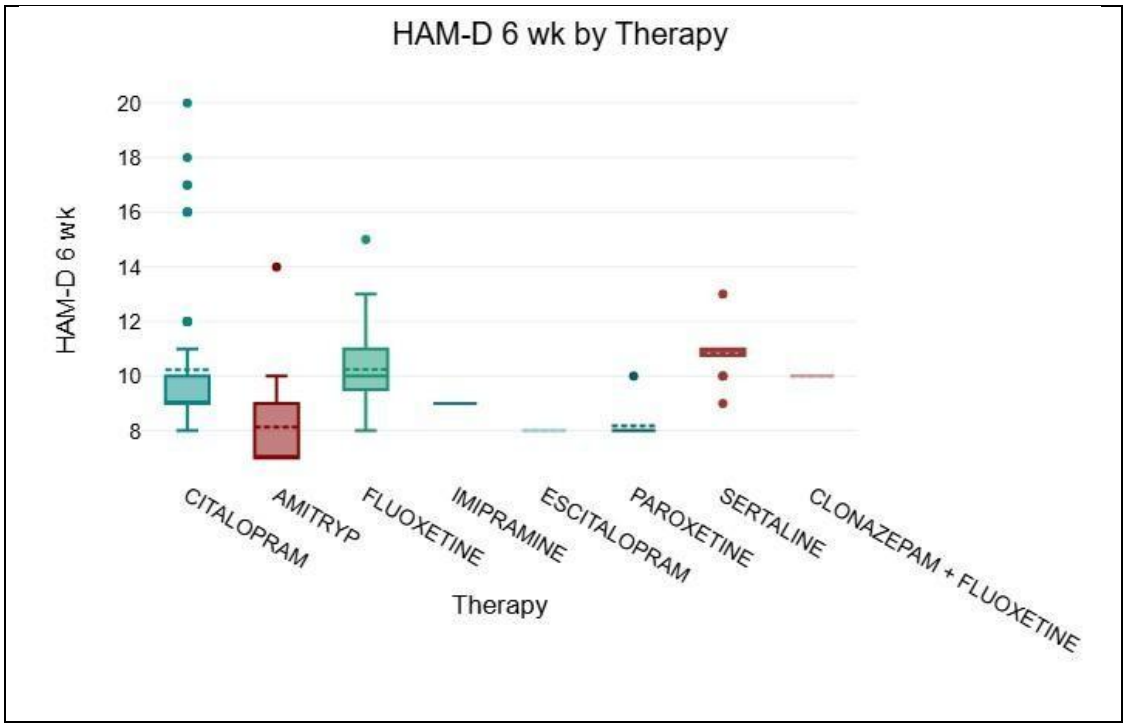


Figure 7: Decreasing pattern of MADR score at follow-up of 6 weeks of antidepressant treatment by particular antidepressant medications (*n*=217)

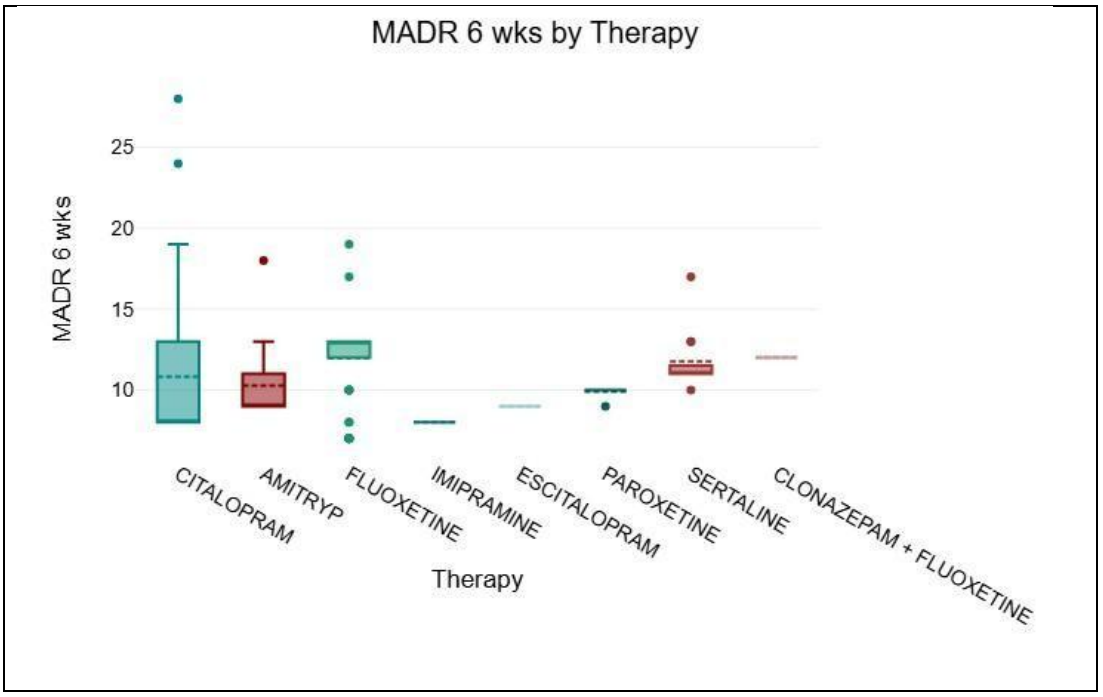


Figure 8: Pattern of severity of depression score in different income group (*n*=217)

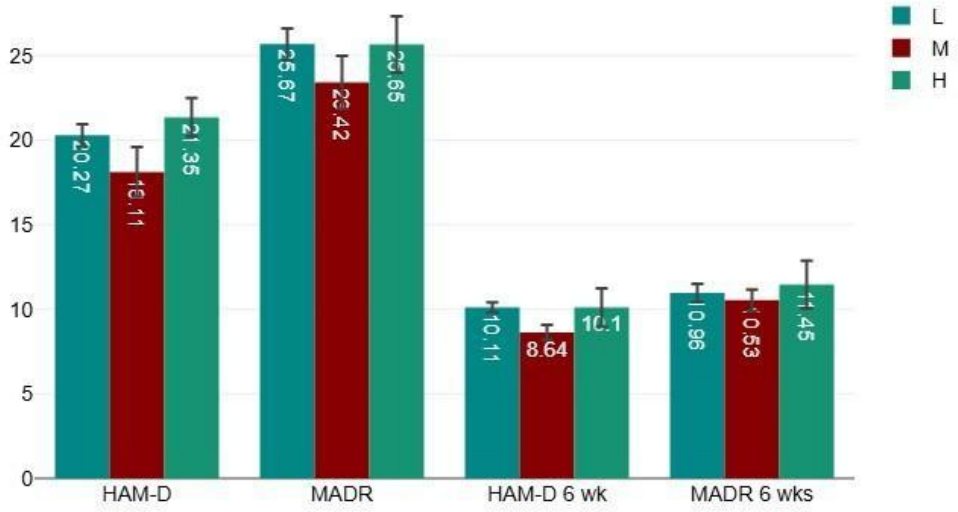


Table 6: Association of severity of depression score with gender ANOVA

	HAM-D	MADR	HAM-D 6 wk	MADR 6 wks	Total	Total
F	**19.73**	**26.12**	**9.67**	**10.92**	**16.61**	**10.87**
M	**19.9**	**24.05**	**9.79**		**16.15**	
				10.89	**16.38**	
	19.81	**25.09**	**9.73**			

	Sum of squares	df	Mean Square	F	p	η^2	η^2_p
HAM-D, MADR, HAM- D 6 wk, MADR 6 wks	34994.48	3	11664.83	1780.18	<.001	0.72	0.89
Gender	45.35	1	45.35	1.02	.313	0	0
RM Factor x Gender	188.99	3	63	9.61	<.001	0	0.04
Residuals (Between Subjects)	9470.59	214	44.26				
Residuals (Within Subjects)	4206.79	642	6.55				

Bonferroni Post-hoc-Tests RM Factor

						95% CI		95% CI
		Mean	Std.	lower limit	upper limit	diff.	Error	t p
HAM-D	MADR	-5.28	0.223	-23.698	<.001	-5.72		-4.84
HAM-D	HAM-D 6 wk	10.08	0.241	41.908	<.001	9.61		10.56
HAM-D	MADR 6 wks	8.92	0.205	43.496	<.001	8.51		9.33
MADR	HAM-D 6 wk	15.36	0.334	46.013	<.001	14.7		16.02
MADR	MADR 6 wks	14.2	0.315	45.143	<.001	13.58		14.82
HAM-D	MADR 6 wks	-1.16	0.137	-8.503	<.001	-1.43	-0.89	6 wk

	Mean diff.	Std. Error	t	p
F-M	0.46	0.45	1.01	.313

Figure 9: Distribution of cost (INR) in prescription following NLEM (2022) for antidepressant medications (*n*=217)

There are 130 sample values in group Y (yes) and 85 sample values in group N (no).

Mean

The average of the value of Cost for the group Y in this sample is 119.88, while it is 106.88 for the group N. This shows that the Y group in this sample has on mean a maximum value for the dependent variable ie **Cost** in rupees than the N group.

Standard deviation

The standard deviation in the descriptive statistics measures the amount of variation or dispersion in a set of the total values. A low standard deviation represents the values are close to the mean, while a higher standard deviation shows the value(s) are distributed out over a broad range. Here, in this study the standard deviation for Y is

14.82 while for N it is 60.32.

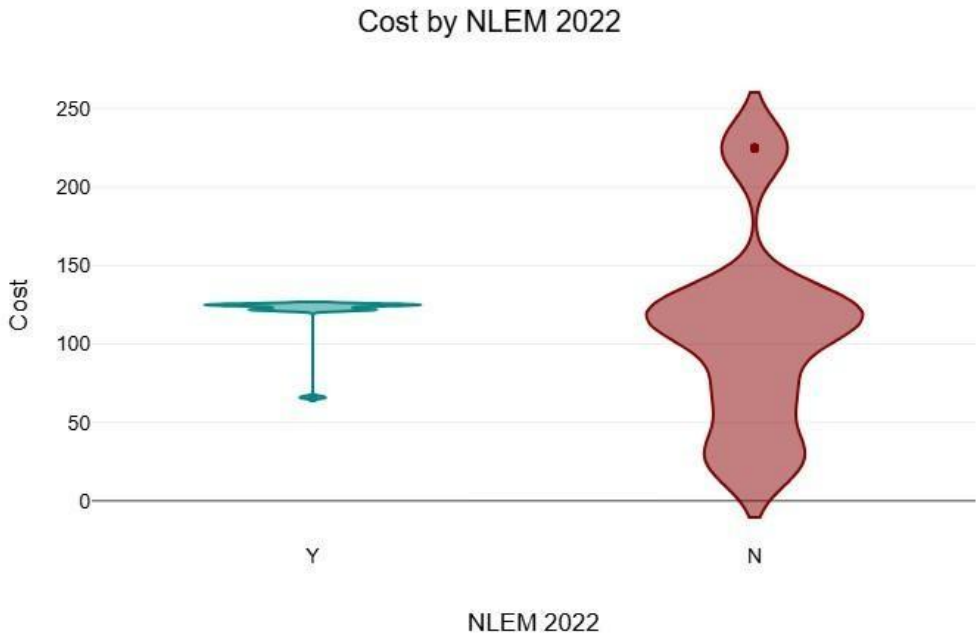


Figure 10. Distribution of Route of drug administration in prescription following NLEM (2022) for antidepressant medications (*n*=217)

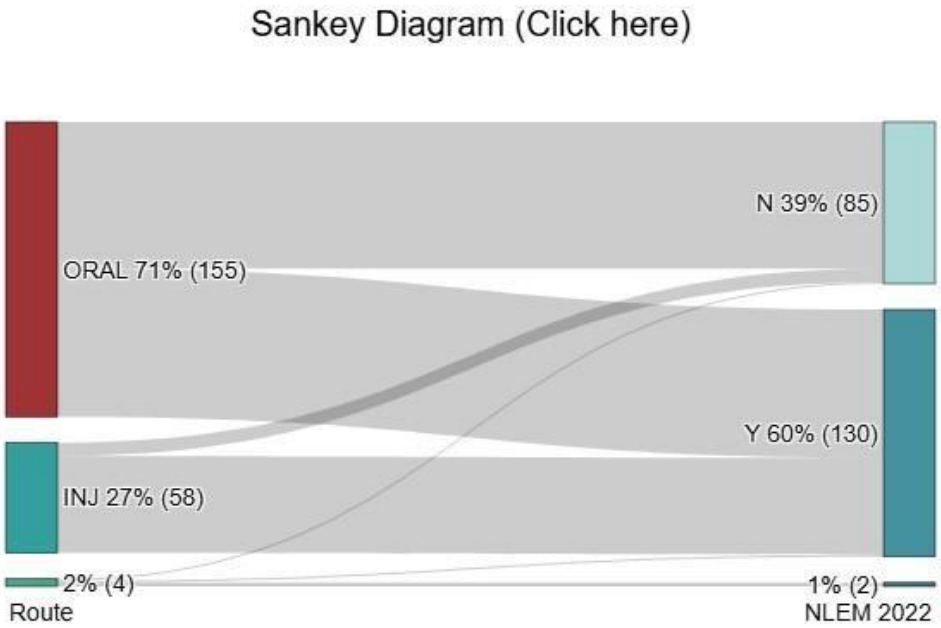


Table 7: Association of severity of depression score with gender using t - test

		n	Mean	Std. Deviation	Std. Error Mean
HAM-D 6 wk	F	110	9.68	2.13	0.2
	M	107	9.79	1.74	0.17

		t	df	p	Cohen's d
HAM-D 6 wk	Equal variances	-0.43	215	.671	
0.06	Unequal variances	-0.43	208.77	.67	
				0.06	

		n	Mean	Std. Deviation	Std. Error Mean
MADR 6 wks	F	110	10.92	3.24	0.31
	M	107	10.87	2.9	0.28

		t	df	p	Cohen's d
MADR 6 wks	Equal variances	0.12	215	.907	0.02
	Unequal variances	0.12	213.62	.907	0.02

The above table shows the statistical key figures of the dependent variable ***HAM-D 6 week*** for the two groups Female and Male populations.

There are 110 sample values in group Female and 107 sample values in group Male.

The average value of HAM-D 6 week for the F group in this sample is 9.68, while it is 9.79 for the Male group. This shows that the F group in this study has a lower value for the ***HAM-D 6 week*** -dependent variable than the Male group.

The standard deviation (S.D.) measures the amount of variation in a set of values. A lower SD means the values are close to the mean value, while a higher SD means the values are distributed out over a wider range. Here, the SD for F is 2.13 and for M it is 1.74.

t-Test for independent samples

The 95% CI-(confidence interval) for their mean difference ranges from -0.64 to 0.41. Since this interval includes 0-zero, it suggesting that the difference in mean value is not statistically significant. In the practical terms, in this study we cannot be confident that the true mean of difference between the two groups is different from the o-(zero).

		n	Mean	Std. Deviation	Std. Error Mean
MADR 6 wks	**F**	110	10.92	3.24	0.31
	M	107	10.87	2.9	0.28

The average value of MAD-R 6 weeks for the F group in this sample is 10.92, while it is 10.87 for the Male group. These results shows that the F group in this sample has on average a higher value for the used in this study of dependent variable *MAD-R 6 weeks* than the M group.

The standard deviation- (S.D.).. measures the amount of variation or dispersion in a set of the values. A lower SD means the values are close to the mean, while a higher SD means the values are Distributed out over a wider range. Here, the SD for F is 3.24 and for M it is 2.9.

t-Test estimation for independent samples followed in the study

		t-	Df-(degreeof freedom	Cohen's value	p d
MADR-6 wks	Equal-variances	0.12	215	.907	0.02
	Unequal variances	0.12	213.62	.907	0.02

The 95% CI-confidence interval for the mean difference observed in the study ranges from -0.78 to 0.88. Since this interval includes 0-zero, it is suggesting that the difference in means is not statistically significant. In the practical terms, in this study, we cannot be confident that the true mean difference between the 2- groups is different from the 0zero.

Table 8: Analysis of Antidepressant prescriptions based on WHO core drug use indicators

S.N	Drug use indicators	Results of analysis
	Total number of Prescription analyzed (n=217) Total number of antidepressant drugs prescribed (n=222)	
1	Average number of antidepressant medicines per prescription	1.02
2	Prescription containing FDC in the study	5 (2.3%)
3	Percentage of prescriptions with drug dosage form	100%
4	Percentage of prescriptions prescribed from NLEM (2022)	130 (59.91%)
5	Percentage of prescription written with generic name	22 (10%)
6	Percentage of prescription written with injectable	58 (26.73%)

DISCUSSION

Chapter 6

DISCUSSION

Patterns of prescription

A rural survey showed that the symptom depression rate was 18% and the depression rate was 27%, while the urban depression was 25.2%[47].

It has been observed that depression in women is twice as common as in men[47]. Numerous studies have shown that more female patients receive antidepressant therapy compared to male colleagues. Evaluation of other antidepressant use using patient data from European countries achieved similar results, indicating that over 65% of the total patient population was female[48]. Similar results were observed in the US, with 70% of the patient group that preserves antidepressant therapy included women[49]. The increased incidence of depression in women compared to men may be directly attributed to the fact that depression in women is twice as widespread as men[50]. This is primarily when the patient group has a range of ages. Studies where antidepressant use was tested in younger children and adolescents found that male proportions were inconsistent among women, resulting in roughly the same proportions[51].

Antidepressants are frequently employed to address various anxiety-related disorders [52]. They may be utilised independently or in conjunction with anxiolytics. A research in South-Africa indicated that anxiolytics accounted for the second highest volume of prescribed nervous system medications[53]. In South Africa, Fluoxetine was the most frequently given SSRI, comprising nearly 63% of all prescriptions, followed by Paroxetine at 28.5%[54]. A South African study indicated that female patients (62.33%) were more often administered SSRIs and SNRIs compared to male patients (54). Sociodemographic characteristics were identified as impacting the type of antidepressant prescribed during the baseline visit. For instance, non-smokers, younger individuals, and those with a higher educational attainment were more inclined to receive a SSRI prescription rather than any alternative antidepressant. The researchers discovered that the recommended antidepressant type was unaffected by parameters such as anxiety severity, current patient functioning, or co-morbidity. The private sector delivers health care to patients possessing a medical aid fund, facilitating access to private (nongovernmental) hospitals and additional health care services. In this area, prescribing is not confined to a specific list of medications; rather, it is regulated by the overall

availability of those drugs in South Africa[55]. In the public health sector, which is stateregulated, prescribing is governed by a catalogue of sanctioned medications referred to as the Essential Drug List (EDL)[56]. The objective of this list is to guarantee a sufficient and secure provision of effective and safe medications to all inhabitants of South Africa in the most economical manner. The criteria for selecting essential pharmaceuticals for Primary Health Care in South Africa were derived from the WHO recommendations for establishing a national EDL[57]. They encompass the subsequent items:

Any included substance must satisfy the requirements of the majority of the population. • Adequate validated scientific evidence regarding efficacy must be accessible. • Any medication incorporated into the EDL must demonstrate a significant safety profile and a favourable risk/benefit ratio. • All products must meet acceptable quality standards and undergo continuous testing. • The primary objective is to include only products with single pharmacologically active ingredients. • Combination products may be included as exceptions when patient adherence is a critical factor or when two pharmacologically active ingredients exhibit synergistic effects. • Products will be catalogued exclusively by their generic names. •[57]. A proposal for the inclusion of a new product in the EDL must be substantiated by scientific data and relevant references highlighting its advantages and benefits over existing products. The conventional treatment guidelines define depression as a persistently low mood (sadness) coupled with anhedonia, diminished interest, and social disengagement. The selection of antidepressants is influenced by concomitant illnesses, such as cardiovascular disease, particularly in the senior population. Tricyclic antidepressants (TCAs) are contraindicated in individuals with cardiovascular illness, whereas SSRIs are used with caution in the geriatric population. The EDL indicates that the primary treatment for MDD consists of the tricyclic anti-depressants amitriptyline and imipramine. The second-line treatment consists of the SSRIs citalopram and fluoxetine[58]. The commercial sector offers a broader range of antidepressants, unlike the state sector, which restricts prescriptions to only two classes. Antidepressant use in people under 20 years of age showed that prescribing patterns in patients under 18 years of age showed that SSRI was 55.91% of antidepressant conjugation and exceeded TCAS, resulting in 32.32% of prescriptions. These two antidepressants accounted for 79.49% of total antidepressant expenditures (54). In another study that tested the prescribing patterns of SSRIs and SNRIs in 19-yearold patients, 440 patients under 19 years of age received antidepressant therapy,

accounting for 6.20% of all antidepressant patients[59]. In 2009, a total of 12,549 antidepressants from patients aged 18 and older were issued from the private health insurance database from a total of 814,540[60].

The study for the disability is one of the few that has investigated the characteristics and characteristics of impairment, as well as its association with mental disorders and its progression over time when viewed from a longitudinal perspective. The total disability scores on either of the two scales that were utilised in the research did not exhibit any significant differences at any of the time points that were considered (baseline, six months, or twelve months). On the other hand, when the scores were classified according to the benchmark disability, which was defined in the Rights of Persons with Disability Act of 2016 as being greater than forty percent, significant differences were observed on the 12-month follow-up. A significantly higher percentage of individuals with the diagnosis of BD fell within the cut-off of benchmark disability in comparison to UD. This provides an explanation for the prevalent clinical practice of issuing a greater number of certificates to patients with BD as opposed to UD[61, 62]. Furthermore, baseline

variations in HAM-D scores were seen between the two groups, which could have contributed to the confusion of the findings. Several research conducted in India on a variety of mental conditions have utilised both measures[63], therefore it is essential to have a solid understanding of the consistency that exists between the two scales. In India, IDEAS is a regularly used tool for determining whether or not an individual is disabled and for providing certification in order to get disability payments. Because of this, it would be worthwhile to investigate the factors in BD that contribute to increased disability in BD patients, which may not be represented in IDEAS.

A number of clinical implications can be drawn from the study. In the case of psychiatric diseases, it is essential to conduct disability evaluations on a frequent basis because it has been observed to improve over time. It is possible that individuals with UD have the same level of disability and dysfunction as those with BD; therefore, they should not be denied the benefit that those in charge of administration and policy should provide. There is a lack of understanding regarding the government programs that are designed to assist those who are in need because mental disability is not evident. In most cases, patients do not make the most of their disability payments, and there is an overall underutilisation of the services[61]. It is essential for physicians to identify the factors that are more likely to result in disability. Once identified, these factors can be targeted for intervention and

rehabilitation measures. Additionally, it is essential to make an estimation of the level of disability by utilising standardised disability scales. This is because the severity of the illness may or may not correspond with the amount of disability. It is therefore not a straightforward process to extrapolate the severity of the illness in order to evaluate the level of disability in all types of psychiatric illnesses. The existing programs that aim to empower people with disabilities do not provide as much assistance to people with mental disabilities as they do to those with physical disabilities. This is most likely due to the fact that it is frequently impossible to forecast the progression of sickness and the disability that is associated with psychiatric illness. It is therefore necessary to take a different strategy in order to empower individuals who are afflicted with psychiatric disorders, which can be just as incapacitating as physical disorders. In light of the findings of our research, we would like to suggest a few ways that are specific to the illness and could perhaps be of more benefit to the persons who are affected by it. In the case of disorders such as unipolar depression, in which the handicap is equally severe but only experienced for a short period of time, the government ought to prioritise the provision of short-term disability help and relief in addition to supporting the patient's
medical expenses. However, the government ought to incorporate disease-specific programs for those who suffer from bipolar depression, which is characterised by a psychiatric handicap that lasts for a comparatively longer period of time. These programs might include longterm rehabilitation and care facilities, vocational training, and disability pensions. There are a number of strengths that the study possesses, including the utilisation of a standardised instrument for diagnosis, the assessment of disability across many types of depressive disorders in a longitudinal manner for more than a year, and the utilisation of numerous scales to verify the concordance. One of the most significant disadvantages of the study is that it does not include people who have mental comorbidities, and the sample size is rather small. Additionally, the distribution of samples among diagnoses is not uniform. In addition, the patients' physical problems, which could also be contributing to their handicap, were not investigated. In addition, the fact that the sample was taken from a tertiary care centre makes it difficult to generalise the findings to the entire population. At some point in the future, it could be beneficial to observe the findings in a large sample size, spanning a variety of diagnoses, and taking into account both psychiatric and physical co-morbidities.

Another study in the US showed that younger patients were significantly more tilted than older patients to prescribe SSRIs[64]. A study conducted in Germany sought to characterize the use of antidepressants and prescribing practices for these drugs in children and adolescents. In Germany, a decrease in SSRI fluoxetine, a limited number of TCAS and herbs in cents showed a study showing an incidence of 1.66 in 1000 children in 2004, 1.57 and 1000 children in 2006[65]. Antidepressants administered among young people were diagnosed with depressive disease in 56.30%. 43.14% of these patients were prescribed antidepressants, and 18.36% increased three prescriptions by 2, 1.88% and 27.62%. Of the 16,886 people who considered antidepressants, 41.72% SSRI, 33.99% TCAS, 15.73% were all prescription antidepressants, and 49.11% were used to carry out the industry. There will be signs. The researchers found that the use of nonadaptive use according to age 40.18% is more common than off-label use due to indication. This appears to be a trend despite the contraindications to use antidepressants in children and adolescents due to increased suicide, as shown in the Black Box Warning. Supervisors warned, particularly in the first few weeks of antidepressant use. However, despite the associated withsuicide, the prevalence of antidepressant use exists[66]. The utilisation of SSRIs, predominantly fluoxetine, escalated during the study period. According to the findings of the majority of the studies, the most prevalent class of antidepressants administered was the SSRIs, which accounted for 32 percent of all prescriptions prescribed[67]. Due to the fact that they have a lower risk of drug interactions and a side effect profile that is substantially less severe, SSRIs are the drugs that are typically recommended first[67]. According to the findings of our research, sertraline was the medication that was prescribed the majority of patient, followed by fluoxetine and escitalopram[68]. In contrast to the findings of the studies conducted by Laxmi et al. and Mishra et al., which revealed that fluoxetine and escitalopram were the most prescribed medicines, the findings of the study conducted by Nayak et al. were similar (69,70,71). It is possible that these variations in findings are the result of variances in the prescription patterns of different centres; nevertheless, it is important to note that these variations do not necessarily reflect national trends. In the current investigation, the next groups of medications that were administered after SSRIs were atypical antipsychotics and TCAs. In the study by Trivedi et al., 83% of patients were prescribed monotherapy and 17% polytherapy; conversely, our analysis identified almost 98 percent of patients receiving monotherapy as medication and only 2% on polytherapy in their treatment. Clonazepam

may have been the favoured benzodiazepine in conjunction with antidepressants, as studies indicate its propensity to enhance the effectiveness of SSRIs and somewhat mitigate their side effects.[67].

Benzodiazepines are habit-forming and must be prescribed judiciously in all patients. These are beneficial only during the initial couple of weeks of depression treatment, especially when used in conjunction with SSRIs, as it was recognised by the NICE guidelines. Consequently, prescribers should prioritise in minimising both the duration and dosage of benzodiazepines group of drugs[72].

The DUR pattern examined in our analysis indicated an average of 1.02 medications per prescription, nearly consistent with the findings of Tejus et al.

Our investigation revealed an average of nearly 2 medications per prescription, with a little proportion of drugs prescribed as FDCs and injectables, similar to the findings of Tejus et al. In a study by Thakkar et al., the percentage of medications from the NLEM was found to be 100%. Conversely, Lahon et al. reported a mere 1 & half % for the NLEM category drugs. In our investigation, the percentages were 60% from NLEM drug prescribed. Our study dispensed drugs by generic names at a rate of 10% only, that is not consistent with the findings of Lahon et al., but Thakkar et al. reported a rate of 76%[73,74,75].

The current investigation also indicated that reductions in the severity of depression symptoms using HAM-D & MADR score. Furthermore, a higher frequency of psychiatric hospitalisations forecasted diminished alterations in psychological and physical quality of life, whilst having a partner anticipated improved changes in psychological and environmental quality of life. Furthermore, alterations in the HAMD score, & MADR score collectively accounted for decrease of the variance in physical health quality of life changes from the baseline to the 6-week follow-up. Changes in the HAM-D score, days lost, and lower education level account for nearly forteen percent of the variance in for total quality of life changes[76].

CONCLUSION

Chapter 7

CONCLUSION

The study examined 217 prescription samples. The mean age of the study participants was 40.39 (SD- 5.96), with a range of 27 to 58 years.

A total of 217 patients suffering from depression disorder were examined inside the psychiatry department. Of these patients, 110 were female, and 53.46 percent were people who were not married. Comorbidities were present in 24.32 percent of patients diagnosed with depressive disorder in this study. The most common comorbidities were hypertension (9.8 percent), migraine (7.4 percent), Parkinson's disease (1.8%), and epilepsy (1.4%). Anti-depressant medications were used in combination form (FDC) by just 2.3% of the people who participated in the investigation. The majority of pharmaceuticals were monotherapies.

For the purpose of this study, participants from both urban and rural settings were recorded in the same manner. A total of 61.75 percent of the population was unemployed at the time of the hospital visit. 65.44% of the participants with a low income, followed by 25.35% with a middle income and 9.22% with a high income. The percentage of patients who were drinkers was 14.29 percent, the percentage of smokers was 10.14 percent, and 18 percent of the patients had a family history of psychiatric diseases.

As an antidepressant, Fluoxetine was administered to 33% of the patients in this study, whereas citalopram was given to 32% of the patients. Additionally, amitriptyline (11%), imipramine (6%), escitalopram (5.5%), sertraline (5.5%), paroxetine (5%), and clonazepam-fluoxetine (2%), were utilised in this research in addition to paroxetine.

At least one ADR was found in 216 of 217 subjects. The most common ADRs are headache, dizziness, dry mouth, sleeplessness, weight gain, sexual dysfunction, diarrhoea, and others.

Antidepressants averaged 1.025 prescriptions. 2.3 percent of drug prescriptions were FDCs. 10% of drug prescriptions were generic. At least 60% of antidepressants prescribed were from NLEM. Parenteral medicines make up 27%.

Among the most commonly utilised medicines were fluoxetine, citalopram, and amitriptyline.

Mean HAMD depression severity scale was 19.82 and while MADR was 25.09.

After 6 weeks of therapy, HAMD dropped to 9.74, while approximately 11 was the mean score of MADR in 6 weeks of the treated patients. Escitalopram and paroxetine were the main drugs that reduced depression severity in our investigation. Detail of the variable like age, gender and other were studied in relation to finding severity of depressive disorders, however, it was not observed statistically significant in this particular study.

This study exhibits some short-comings that require attention. The sample size of this prescription-based study was very limited; therefore, subsequent studies utilising bigger representative samples may yield enhanced understanding of the efficacy of the drugs & quality of life over time of the patients. This observational study included patients with all form of depressive illness; hence, the findings may not precisely reflect a particular subgroup of persons with MDD. Moreover, although we aimed to evaluate many variables previously studied like gender, education, profession, co-morbidities etc, we recognise that not all factors affecting HAM-D & MADR score were addressed. Future study should include an additional subjective assessment of depression symptoms, as QOL is thus a subjective metric.

A further drawback of the present investigation is that the follow-up duration was confined to the acute therapy phase. Prolonged follow-ups may provide deeper insights into the QOL improvements for patients with depressive disorder, thereby can enhance personalised care & effectiveness of the medication.

REFERENCES

REFERENCES

1. WHO International Working Group for Drug Statistics Methodology. Introduction to Drug Utilization Research [Internet]. Oslo, Norway: WHO Collaborating Centre for Drug Utilization Research and Clinical Pharmacological Services; 2003.
2. Deshmukh SA, Ismail TSES. Evaluation of Psychotropic Drugs Use Pattern among Out Patients Attending Psychiatry Department at Government Medical College and Hospital, Nagpur: A Cross Sectional Study. International Journal of Pharma and BioSciences. 2012 July; 3(3): 428–36.
3. Wubetu M, Derebe D, Mulaw T, Yimer T, Hailu G. Assessment of Drug Prescription Pattern in Two District Hospitals, Northwest Ethiopia. Journal of Health Education Research & Development. 2018; 6(1): 1-4.
4. Thakkar KB, Jain MM, Billa G, Joshi A, Khobragade AA. A Drug Utilization Study of Psychotropic Drugs Prescribed in the Psychiatry Outpatient Department of a Tertiary Care Hospital. Journal of Clinical and Diagnostic Research. 2013 Dec; 7(12):2759-64.
5. World Health Organization. Improving access and use of psychotropic medicinesWHO mental health policy and service guidance package - module 10 https://www.who.int/mental_health/policy/services/essentialpackage1v10/en/ 6. Murthy R. Mental Health Programme in the 11th five-year plan. Indian J Medl Res. 2007; 11:707-12.
7. Sharma P, Das S, Deshpande S. An estimate of the monthly cost of two major mental disorders in an Indian metropolis. Indian J Psychiatry. 2006; 48:143-8.
8. World Health Organization. The World Health Report 2001- Mental Health: New understanding, new hope. Geneva; 2001. Available from: http:// www.who.int/whr/2001/en/
9. American Psychological Association https://dictionary.apa.org/mental-disorder
10. Scangos KW, State MW, Miller AH, Baker JT, Williams LM. New and emerging approaches to treat psychiatric disorders. Nature Medicine. 2023 Feb;29(2):317-33.

11. Iannuzzo RW, Jaeger J, Goldberg JF, Kafantaris V, Sublette ME. Development and reliability of the HAM-D/MADRS interview: an integrated depression symptom rating scale. Psychiatry research. 2006 Nov 29;145(1):21-37.
12. Funk, C.S.M.; Hart, X.M.; Gründer, G.; Hiemke, C.; Elsner, B.; Kreutz, R.; Riemer, T.G. Is therapeutic drug monitoring relevant for antidepressant drug therapy? Implications from a systematic review and meta-analysis with focus on moderating factors. Front. Psychiatry 2022, 13, E184.
13. Uchida, N.; Chong, M.Y.; Tan, C.H.; Nagai, H.; Tanaka, M.; Lee, M.S.; Fujii, S.; Yang, S.Y.; Si, T.; Sim, K.; et al. International study on antidepressant prescription pattern at 20 teaching hospitals and major psychiatric institutions in East Asia: Analysis of 1898 cases from China, Japan, Korea, Singapore and Taiwan. Psychiatry Clin. Neurosci. 2007, 61, 522–528.
14. Hofmann, S. G., Asnaani, A., Vonk, I. J. J., Sawyer, A. T., & Fang, A. (2012). The Efficacy of Cognitive Behavioral Therapy: A Review of Meta-analyses. Cognitive Therapy and Research, 36(5), 427–440.
15. Cuijpers, P., Karyotaki, E., Weitz, E., Andersson, G., Hollon, S. D., van Straten, A. (2016). The effects of psychotherapies for major depression in adults on remission, recovery and improvement: a meta-analysis. Journal of Affective Disorders, 210217.
16. Mars, B., Heron, J., Kessler, D., Davies, N. M., Martin, R. M., Thomas, K. H., & Gunnell, D. (2016). Influences on antidepressant prescribing trends in the UK: 1995–2011. Social Psychiatry and Psychiatric Epidemiology, 51(2), 319–327.
17. Chisholm D. Choosing cost-effective interventions in psychiatry: results from the CHOICE programme of the World Health Organization. World Psychiatry. 2005 Feb;4(1):37-44. PMID: 16633504; PMCID: PMC1414721.
18. Chand, S.P.; Arif, H.; Kutlenios, R.M. Depression (Nursing); StatPearls Publishing: Treasure Island, FL, USA, 2021.
19. Chadda RK. Global burden of mental disorders: meeting the challenge. Annals of the National Academy of Medical Sciences (India). 2016 Jan;52(01):039-55.
20. Gutiérrez-Rojas L, Porras-Segovia A, Dunne H, Andrade-González N, Cervilla JA. Prevalence and correlates of major depressive disorder: a systematic review.

Brazilian Journal of Psychiatry. 2020 Aug 3;42:657-72.

21. Marx W, Penninx BW, Solmi M, Furukawa TA, Firth J, Carvalho AF, Berk M. Major depressive disorder. Nature Reviews Disease Primers. 2023 Aug 24;9(1):44.
22. Zaki NF, Spence DW, BaHammam AS, Pandi-Perumal SR, Cardinali DP, Brown GM. Chronobiological theories of mood disorder. European archives of psychiatry and clinical neuroscience. 2018 Mar;268:107-18.
23. Hagen EH. Evolutionary theories of depression: a critical review. The Canadian Journal of Psychiatry. 2011 Dec;56(12):716-26.
24. Schatzberg AF. New approaches to managing psychotic depression. Journal of Clinical Psychiatry. 2003 Jan 1;64(1):19-23.
25. Richardson K, Barkham M. Recovery from depression: a systematic review of perceptions and associated factors. Journal of mental health. 2020 Jan 2;29(1):103-15.
26. Kivlichan AE, Praecht A, Wang C, George TP. Substance-induced mood disorders: a scoping review. Current Addiction Reports. 2024 Feb;11(1):1-8.
27. Casey P, Bailey S. Adjustment disorders: the state of the art. World Psychiatry. 2011 Feb;10(1):11.
28. Thom R, Silbersweig DA, Boland RJ. Major depressive disorder in medical illness: a review of assessment, prevalence, and treatment options. Psychosomatic medicine. 2019 Apr 1;81(3):246-55.
29. Bayes A, Parker G. How to choose an antidepressant medication. Acta Psychiatrica Scandinavica. 2019 Mar;139(3):280-91.
30. Gartlehner G, Wagner G, Matyas N, Titscher V, Greimel J, Lux L, Gaynes BN, Viswanathan M, Patel S, Lohr KN. Pharmacological and non-pharmacological treatments for major depressive disorder: review of systematic reviews. BMJ open. 2017 Jun 1;7(6):e014912.
31. Dupuy JM, Ostacher MJ, Huffman J, Perlis RH, Nierenberg AA. A critical review of pharmacotherapy for major depressive disorder. International Journal of Neuropsychopharmacology. 2011 Nov 1;14(10):1417-31.

32. Richelson E. Pharmacology of antidepressants—characteristics of the ideal drug. InMayo Clinic Proceedings 1994 Nov 1 (Vol. 69, No. 11, pp. 1069-1081). Elsevier.
33. Karunarathna I, Jayawardana A, Bandara S. Comprehensive Review of Antidepressant Therapy.
34. Gage DS, Priefer VE, Priefer R. A Narrative Review: Serotonin Reuptake Inhibitors and the Risk of Suicidal Ideation in Adolescents. Adolescents. 2025 Feb 5;5(1):5.
35. Lense XM, Hiemke C, Funk CS, Havemann-Reinecke U, Hefner G, Menke A, Mössner R, Riemer TG, Scherf-Clavel M, Schoretsanitis G, Gründer G. Venlafaxine's therapeutic reference range in the treatment of depression revised: a systematic review and meta-analysis. Psychopharmacology. 2024 Feb;241(2):275-89.
36. Martone A, Possidente C, Fanelli G, Fabbri C, Serretti A. Genetic factors and symptom dimensions associated with antidepressant treatment outcomes: clues for new potential therapeutic targets?. European Archives of Psychiatry and Clinical Neuroscience. 2024 Aug 27:1-5.
37. Solmi M, Miola A, Capone F, Pallottino S, Højlund M, Firth J, Siskind D, Holt RI, Corbeil O, Cortese S, Dragioti E. Risk factors, prevention and treatment of weight gain associated with the use of antidepressants and antipsychotics: a state-of-the-art clinical review. Expert Opinion on Drug Safety. 2024 Oct 2;23(10):1249-69.
38. Hess D. 2004. Retrospective Studies and Chart Reviews. Respiratory Care 49:1171–1174.
39. Truter I, Kotze T. 2007. Prescribing of tricyclic antidepressant drugs in a South African primary care patient population. International Journal of Pharmacy Practice 14: 301-310
40. Kairuz TE, Truter I, Hugo J, Foxcroft CD. 2003 Prescribing patterns of tricyclic and selective serotonin reuptake inhibitor antidepressants among a sample of adolescents and young adults. Pharmacoepidemiol Drug Safety 12:379–82.
41. Ionescu DF, Niciu MJ, Henter ID, Zarate Jr CA. Defining anxious depression: a review of the literature. CNS spectrums. 2013 Oct;18(5):252-60.

42. Davidson J, Turnbull CD, Strickland R, Miller R, Graves K. The Montgomery ‐ Åsberg Depression Scale: reliability and validity. Acta psychiatrica scandinavica. 1986 May;73(5):544-8.

43. Iannuzzo RW, Jaeger J, Goldberg JF, Kafantaris V, Sublette ME. Development and reliability of the HAM-D/MADRS interview: an integrated depression symptom rating scale. Psychiatry research. 2006 Nov 29;145(1):21-37.

44. Edwards IR, Aronson JK. Adverse drug reactions: definitions, diagnosis, and management. The lancet. 2000 Oct 7;356(9237):1255-9.

45. Muenchen RA. The popularity of data analysis software. URL http://r4stats. com/popularity. 2012.

46. McHugh ML. The chi-square test of independence. Biochemia medica. 2013 Jun 15;23(2):143-9.

47. Wu Y, Su B, Chen C, Zhao Y, Zhong P, Zheng X. Urban-rural disparities in the prevalence and trends of depressive symptoms among Chinese elderly and their associated factors. Journal of Affective Disorders. 2023 Nov 1;340:258-68.

48. Van de Velde S, Bracke P, Levecque K. Gender differences in depression in 23 European countries. Cross-national variation in the gender gap in depression. Social science & medicine. 2010 Jul 1;71(2):305-13.

49. Serna MC, Cruz I, Real J, Gascó E, Galván L. Duration and adherence of antidepressant treatment (2003 to 2007) based on prescription database. European Psychiatry. 2010 May;25(4):206-13.

50. Kuehner C. Why is depression more common among women than among men?. The lancet psychiatry. 2017 Feb 1;4(2):146-58.

51. Hetrick SE, McKenzie JE, Bailey AP, Sharma V, Moller CI, Badcock PB, Cox GR, Merry SN, Meader N. New generation antidepressants for depression in children and adolescents: a network meta analysis. Cochrane Database of Systematic Reviews. 2021(5).

52. Riordan DM, Singhal D. Anxiety related disorders: An overview. Journal of paediatrics and child health. 2018 Oct;54(10):1104-9.

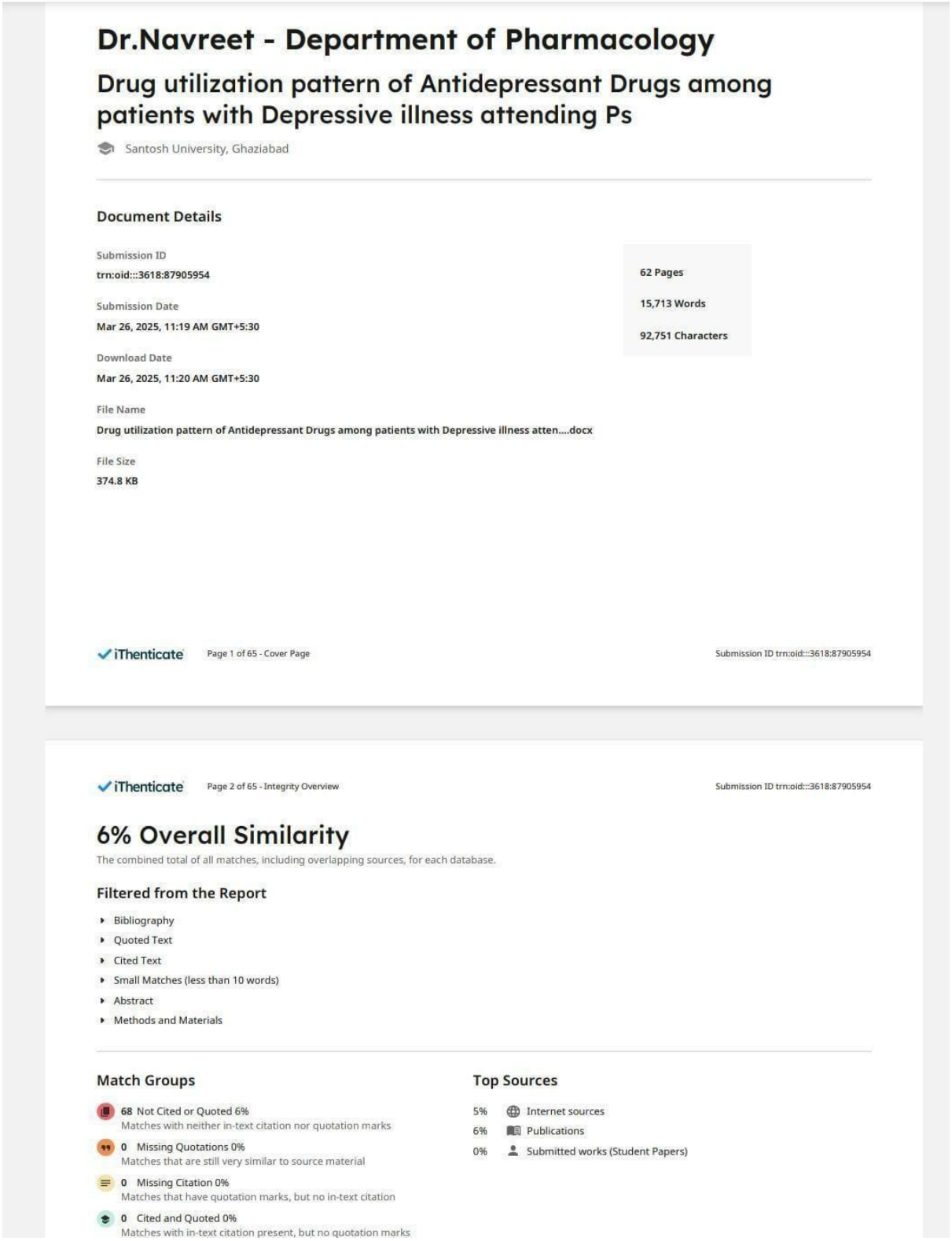
53. Tomlinson M, Grimsrud AT, Stein DJ, Williams DR, Myer L. 2009. The epidemiology of major depression in South Africa: results from the South African stress and health study. South African Medical Journal 99:367-373.
54. Bagwathpersad N. *Antidepressant prescribing in Gauteng: A public sector drug utilization review* (Master's thesis, University of the Witwatersrand, Johannesburg (South Africa)).
55. Morgan R, Ensor T, Waters H. Performance of private sector health care: implications for universal health coverage. The lancet. 2016 Aug 6;388(10044):606-12.
56. Mancino S. Internship Report at the EMCDDA's Public Health Unit-Insights into the Medical Use of Psychedelic Substances in the EU: regulatory frameworks, public health challenges and future directions.
57. Sooruth UR, Sibiya MN, Sokhela DG. The use of Standard Treatment Guidelines and Essential Medicines List by professional nurses at primary healthcare clinics in the uMgungundlovu District in South Africa. International journal of Africa nursing sciences. 2015 Jan 1;3:50-5.
58. Yekehtaz H, Farokhnia M, Akhondzadeh S. Cardiovascular considerations in antidepressant therapy: an evidence-based review. The Journal of Tehran University Heart Center. 2013 Oct 28;8(4):169.
59. Sun S. *Attention-deficit/hyperactivity disorder and adverse health outcomes: from association to prevention* (Doctoral dissertation, Karolinska Institutet (Sweden)).
60. Bagwathpersad N. *Antidepressant prescribing in Gauteng: A public sector drug utilization review* (Master's thesis, University of the Witwatersrand, Johannesburg (South Africa)).
61. Singh J, Sood M, Chadda RK, Singh V, Kattula D. Mental health issues and coping among health care workers during COVID19 pandemic: Indian perspective. Asian journal of psychiatry. 2021 Jul 1;61:102685.
62. Jadhav KK, Daouk J, Kurkinen K, Kraav SL, Eriksson P, Tolmunen T, Kanninen KM. Blood cytokines in major depressive disorder in drug-naïve adolescents: A systematic review and meta-analysis. Journal of Affective Disorders. 2024 Nov 25.
63. Goyal E, Chaudhury S, Saldanha D. Psychiatric comorbidity in patients undergoing hemodialysis. Industrial psychiatry journal. 2018 Jul 1;27(2):206-12.

64. Darowski A, Chambers SA, Chambers DJ. Antidepressants and falls in the elderly. Drugs & aging. 2009 May;26:381-94.
65. Dörks M. *Routinedatenbasierte Untersuchungen zum Off-Label-Use in der ambulanten Versorgung* (Doctoral dissertation, Universität Bremen).
66. Noel C. Antidepressants and suicidality: History, the black-box warning, consequences, and current evidence. Mental Health Clinician. 2015 Sep 1;5(5):202-11.
67. Tripathi A, Avasthi A, Desousa A, Bhagabati D, Shah N, Kallivayalil R, et al. Prescription pattern of antidepressants in five tertiary care psychiatric centres of India. Indian J Med Res. 2016;143(4):507.
68. Jyotiranjan N, Prasanna SS, Priti D. Current Trends in Utilization of Antidepressants in a Tertiary Care Teaching Hospital: An Observational Study. IJCRR. 2021;13(15):127-32.
69. Chattar KB, Karve A, Subramanyam A, Tondare S. Prescription pattern analysis of antidepressants in psychiatric outpatient department of tertiary care hospital in India. Asian J Pharm Clin Res. 2016;9(4).
70. Laxmi P, Mounika S, Babu BJ, Kishore P. An Observational Study of drug use patterns in Depression patients in an Outpatient Department. J Med Sci Clin Res. 2019;7(9).
71. Mishra S, Trupti S, Mohanty M. Patterns of prescription & efficacy evaluation of Antidepressants in a tertiary care teaching hospital in Eastern India. Asian J Pharm Clin Res. 2012;5:193-6.
72. Grover S, Avasth A, Kalita K, Dalal P, Rao G, Chadda R, et al. IPS multicentric study: Antidepressant prescription patterns. Indian J Psychiatry. 2013;55(1):41.
73. Tejus A, Saxena SK, Dwivedi AK, Salmani MF, Pradhan S. Analysis of the prescription pattern of psychotropics in an outpatient department of a general hospital psychiatry unit. Med J Armed Forces India. 2022;78(1):74-9.
74. Thakkar KB, Jain MM, Billa G, Joshi A, Khobragade AA. A Drug Utilization Study of Psychotropic Drugs Prescribed in the Psychiatry Outpatient Department of a Tertiary Care Hospital. J Clin Diagn Res. 2013;7(12):2759-64.

75. Lahon K, Shetty HM, Paramel A, Sharma G. A retrospective drug utilization study of antidepressants in the psychiatric unit of a tertiary care hospital. J Clin Diagnost Res. 2011;5:1069-75.
76. Dogaru IA, Puiu MG, Manea M, Dionisie V. Current perspectives on pharmacological and non-pharmacological interventions for the inflammatory mechanism of unipolar depression. Brain Sciences. 2022 Oct 18;12(10):1403.

ANNEXURE

ANNEXURE-1 Plagiarism Certificate



Dr.Navreet - Department of Pharmacology

Drug utilization pattern of Antidepressant Drugs among patients with Depressive illness attending Ps

Santosh University, Ghaziabad

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ANNEXURE-2 ETHICAL CLEARANCE

SANTOSH
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F. No. SU/R/2023/2489[28] Dated: 26.09.2023

Subject: Grant of Ethical Clearance for **Thesis Protocol** Topic **"DRUG UTILIZATION PATTERN OF ANTIDEPRESSANT DRUGS AMONTS PATIENTS WITH DEPRESSIVE ILLNESS ATTENDING PSYCHIATRY OPD IN A TERITARY CARE TEACHING HOSPITAL",** submitted by **Dr. NAVREET,** MD/MS student of Batch 2022-2023, Department of **PHARMACOLOGY**.

*****

With reference to his/her request for grant of Ethical Clearance for the Thesis Protocol entitled **"DRUG UTILIZATION PATTERN OF ANTIDEPRESSANT DRUGS AMONTS PATIENTS WITH DEPRESSIVE ILLNESS ATTENDING PSYCHIATRY OPD IN A TERITARY CARE TEACHING HOSPITAL", Dr. NAVREET** is informed that the **Thesis Protocol** submitted by him/her was considered by the **Screening Committee** of the Santosh Medical College & Hospital in its meetings held on 17.07.2023 to 28.07.2023. The recommendations of the **Screening Committee** were considered in detail by the **Institutional Ethics Committee** in its meeting held on **23.09.2023** and the same was **approved** by the **Ethics Committee**.

He /She is informed accordingly for further necessary action.

[Dr. NARESH SHARMA]
REGISTRAR

SANTOSH "DEEMED TO BE UNIVERSITY" REGISTRAR GHAZIABAD, NCR DELHI

Dr. NAVREET
MD/MS student of batch 2022-2023
Department of PHARMACOLOGY
Email: navreetthakran786@gmail.com

Copy to:

1. The Vice Chancellor
2. The Dean, SMC&H
3. The Dean – Academics
4. The Dean – Research
5. The Director - IQAC
6. Dr. Shaktibala Dutta (Guide)
7. HOD of PHARMACOLOGY

ANNEXURE-3
CONSENT FORM OF THE PATIENT

Serial No	Date:
Patient's Name:	Age/Sex: -
Father's/Husband Name: -	

I have been explained in my vernacular language about the details of the study to be pursued in the common interest titled as **"Drug Utilization Pattern of Antidepressant drugs among Patients with Depressive Illness Attending Psychiatry OPD in a Tertiary Care Teaching Hospital"** and

1. I understand the purpose of the study and I have the right to withdraw from the study at any point of time during the research and can decline to answer any particular question if it offends privacy in any form without losing the right to be treated.
2. I understand that my participation in this study will be kept confidential and primarily meant for research and benefit of the society.
3. I also understand that if there is any problem with any of the tests or measurements taken, I will be informed, and the report will be kept confidential.
4. I do hereby give my consent voluntarily without any inducement to take part in the study titled as above and I have no objection to the use of data for any publication.

Signature/ Thumb Impression of patient

Name &Signature of the investigator

Name & Address of the patient

1. Witness name & signature
2. Witness name & signature

Contact for further information If you have any other queries about the study, please revert and contact:

Student Name: Dr. Navreet
Department of Pharmacology
Santosh Medical College & Hospital,
Ghaziabad, Uttar Pradesh
Contact number: 9971029517

ANNEXURE-4

संतोष विश्व विद्याऱय (भेषजगणु विज्ञान विभाग)

सहमततपत ्र

क्रम ा ा क स ख्य :	त रीख:
मरीज क न म:	आयु/लऱग :
पऩत /ऩतत क न म:	

मझ ु अऩनी स्थ नीय भ ष में **" एक क क क क क** **क** " शीषकष स स म न्य हहत में ककए ज न व ऱ अध्ययन क पववरण क ब र में समझ य गय है और

1. मैं अध्ययन क उद्द श्य को समझत ह ा ा और मझ ु शोध क दौर न ककसी भी समय अध्ययन स हटन क अधधक र है और इऱ ज क अधधक र को खोए बबन ककसी भी पवशष प्रश्न क उत्तर द न स इनक र कर सकत ह ा ा यहद यह ककसी भी रूऩ में गोऩनीयत को ठ स ऩह च त है।
2. मैं समझत /समझती ह ा ा कक इस अध्ययन में म री भ गीद री को गोऩनीय रख ज एग और इसक मख्यु उद्द श्य शोध और सम ज क ऱ भ क लऱए है।
3. मैं यह भी समझत ह ा ा कक यहद ककसी भी ऩरीा ण य म ऩ में कोई समस्य आती है, तो मझ ु सधचत ककय ज एग , और ररऩोटष को गोऩनीय रख ज एग ।
4. मैं उऩरोक्त शीषकष क अध्ययन में भ ग ऱ न क लऱए बबन ककसी प्रऱोभन क स्व च्छ स अऩनी सहमतत द त ह ा ा और मझ ु ककसी भी प्रक शन क लऱए डट क उऩयोग ऩर कोई आऩत्त नही है।

रोगी क हस्त ा र/अग ठ क

तनश न अन्व षक क न म और

हस्त ा र रोगी क न म और ऩत

1. गव ह क न म और हस्त ा र 2.
गव ह क न म और हस्त ा र

अधधक ज नक री और अध्ययन क ब र में आन्नक कोई अन्य प्रश्न हैं, तो कृ न्नय सन्न कष कर **छात्र का नाम**: . **विभाग**: भ षजगणु पवां न स तोष म डडकऱ कॉऱ ज और अस्नत ऱ, ग त्जय ब द, उत्तर प्रद श

संपकक नंबर: 9971029517

ANNEXURE-5

DATA SHEET

NAME:	DATE:
AGE:	HEIGHT:
WEIGHT:	RELIGION:
OCCUPATION:	MARITAL STATUS:
PSYCHIATRIC ILLNESS: Types of Depression	EDUCATIONAL STATUS:
Antidepressant Drugs: 1. 2. 3.	OTHER DRUGS: 1. 2. 3.
Severity of Depression at the time visit 1. HAM-D score 2. MADR score	**Severity of Depression at 6 weeks after the treatment** 1. HAM-D score 2. MADR score

Drug dose: **Route of drug administration/dosage form:**

Social habit: **Brand name/ Generic name:**

Medical history: **Drug total cost:**

Co-morbidities:

Adverse Drug reactions: